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RESPIRATORY CARE

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- Comparison of Nebulizer Systems in COPD Patients
- Auto-PEEP Associated with High O_2 Flow in Manual Resuscitators
- Work of Breathing and Pressure-Time Product on Pressure Support Ventilation, Continuous Positive Airway Pressure, and T-Piece
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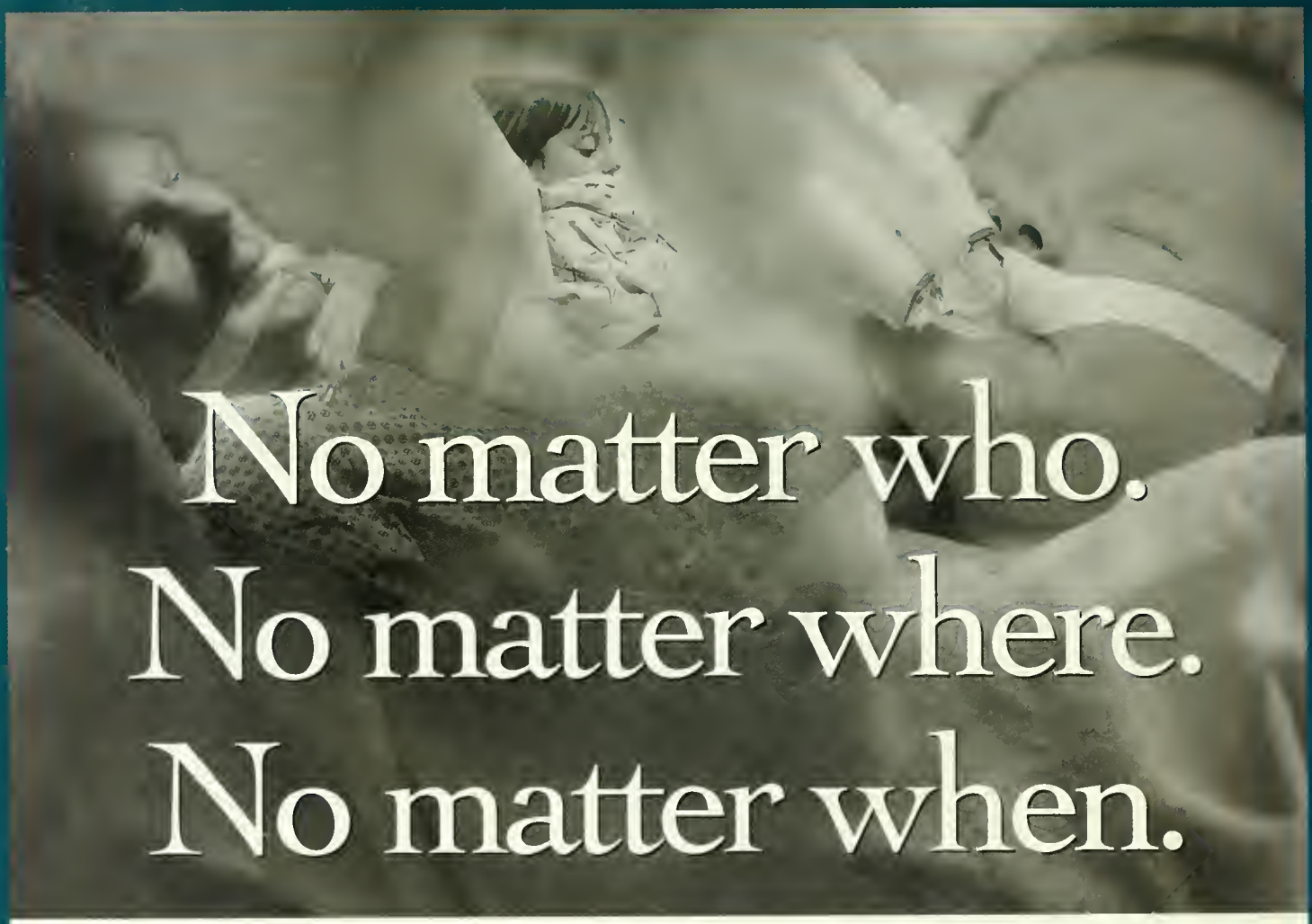

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Editorials, Commentaries, and Reviews To Note

Quality of Health Care. Part 1: Quality of Care—What Is It? (Special Article)—D Blumenthal. N Engl J Med 1996;335(12):891-894. *See the related editorial:* ***Quality and the Medical Marketplace—Following Elephants*** *M Angell, JP Kassirer. N Engl J Med 1996;335(12):883-885.*

The Food and Drug Administration's Regulation of Tobacco Products (Special Report)—DA Kessler, AM Witt, PS Barnett, MR Zeller, SL Natanblut, JP Wilkenfeld, CC Lorraine, LJ Thompson, WB Schultz. N Engl J Med 1996;335(13):988-994.

The National Committee for Quality Assurance (Health Policy Report)—JK Iglehart. N Engl J Med 1996;335(13):995-999.

Quality of Health Care—Part 2: Measuring Quality of Care—RH Brook, EA McGlynn, PD Cleary. N Engl J Med 1996;335(13):966-970.

A Cohort Study on Childhood Asthma Admissions and Re-Admissions—T To, P Dick, W Feldman, R Hernandez. Pediatrics 1996;98(2):191.

BACKGROUND: Admissions to hospitals for childhood asthma seem to be increasing, even though admissions for other childhood conditions are decreasing. We studied admissions and re-admissions for childhood asthma in Ontario in an attempt to uncover factors relating to the admission patterns. METHODS: Using the hospital discharge data from the Canadian Institute for Health Information, 28,646 children with diagnoses of asthma were identified from April 1, 1989, to March 31, 1992. RESULTS. The admission rates for asthma among children in Ontario showed a 14.8% decrease from 1987 to 1992. This decline was observed primarily in 5- to 17-year-olds. Younger children had a 4-fold risk of hospital admission for asthma. In the 4 years studied, 10,427 children (36.4%) were re-admitted at least once, representing 22,114 re-admissions, 16,146 (73.2%) of which were for asthma. The 6-month probabilities of re-admission for asthma were 20.0% (0- to 4-year-olds) and 11.7% (5- to 17-year-olds). The estimated relative risks (RRs) indicated that younger children had a significantly higher risk of re-admission for asthma (RR, 1.38; 95% confidence interval, 1.30 to 1.46) or asthma-related causes (RR, 5.02; 95% confidence interval, 4.16 to 6.05). CONCLUSIONS: The observed increasing trend in admissions for asthma among children in the 1970s and 1980s leveled off in the early 1990s. The declining admission rates were largely caused by the lower admission rates among school-aged children from 5 to 17 years. The relatively high admission and re-admission rates of preschool children are still a concern. Further research is necessary to examine factors that influence admissions for asthma among young children.

A Controlled Trial of Dexamethasone To Prevent Bronchopulmonary Dysplasia in Surfactant-Treated Infants—A Rastogi, SM Akintorin, ML Bez, P Morales, RS Pildes. Pediatrics 1996;98(2):204.

BACKGROUND: Surfactant therapy now has a well-established role in the treatment of neonates with respiratory distress syndrome but has failed to reduce the incidence of bronchopulmonary dysplasia (BPD). We conducted a double-blind, placebo-controlled trial to test the hypothesis that dexamethasone therapy given during the first 12 days of life to very low-birthweight infants would be synergistic to surfactant in preventing BPD. METHODS: Seventy surfactant-pretreated infants (700-1,500 g) who had severe respiratory distress syndrome (a/A ratio, 0.18 ± 0.10; mean airway pressure, 11.1 ± 1.9 cm H_2O; fraction of inspired oxygen, 0.81 ± 0.22) were enrolled to receive a 12-day course of dexamethasone (n = 36) or saline placebo (n = 34) starting within the first 12 hours after birth. The starting dose of dexamethasone was 0.5 mg/kg per day, and it was tapered progressively. RESULTS: Ventilator variables at 5 to 14 days were significantly improved in those infants who received dexamethasone compared with those who received the placebo. The effect seemed to be more marked in infants weighing < 1,250 g at birth. Significantly more infants could be extubated by 14 days of age in the dexamethasone group (26 of 32 vs 14 of 32). Dexamethasone therapy reduced the incidence of BPD at 28 days (odds ratio, 0.1; 95% confidence interval, 0.03 to 0.3) and eliminated BPD at 36 weeks' postconceptional age. Dexamethasone-treated infants had greater weight loss at 14 days (12.9 ± 6.4% vs 3.7 ± 8.6%, respectively) and higher blood pressures from days 3 to 10. However, no differences were seen in time to regain birthweight, hypertension (1 infant in each group), or incidence of intraventricular hemorrhage. CONCLUSIONS: We found an additive effect between dexamethasone and surfactant in improving pulmonary status and reducing the incidence of BPD. Compared with the placebo, dexamethasone therapy was more effective in reducing the incidence of BPD in surfactant-pretreated very low birthweight infants.

Self-Perceived Health Status and Health-Related Quality of Life of Extremely Low-Birthweight Infants at Adolescence—S Saigal, D Feeny, P Rosenbaum, W Furlong, E Burrows, B Stoskopf. JAMA 1996;276(6):453.

OBJECTIVES: To estimate and to compare the self-assessed health status and health-related quality of life of extremely low-birthweight (ELBW) and control infants during adolescence. DESIGN: Prospective, observational study of an inception cohort with a concurrent control group. SETTING: Geographically defined region in central-west Ontario. PARTICIPANTS: We interviewed 141 (83%) of 169 ELBW survivors born between 1977 and 1982 and 124 (86%) of 145 controls aged between 12 and 16 years. In addition, proxy responses obtained from parents were used for 9 severely impaired teenagers. MAIN OUTCOME MEASURES: Assessments of health status (6

WHICH

HUMIDIFICATION SYSTEM PROVIDES
THE OPTIMUM LEVEL OF HUMIDITY

WHICH

MAINTAINS THE MUCOCILIARY
TRANSPORT SYSTEM IN PEAK CONDITION

WHICH

PRESERVES NATURAL RESISTANCE
TO THE DEVELOPMENT OF NOSOCOMIAL
PNEUMONIA

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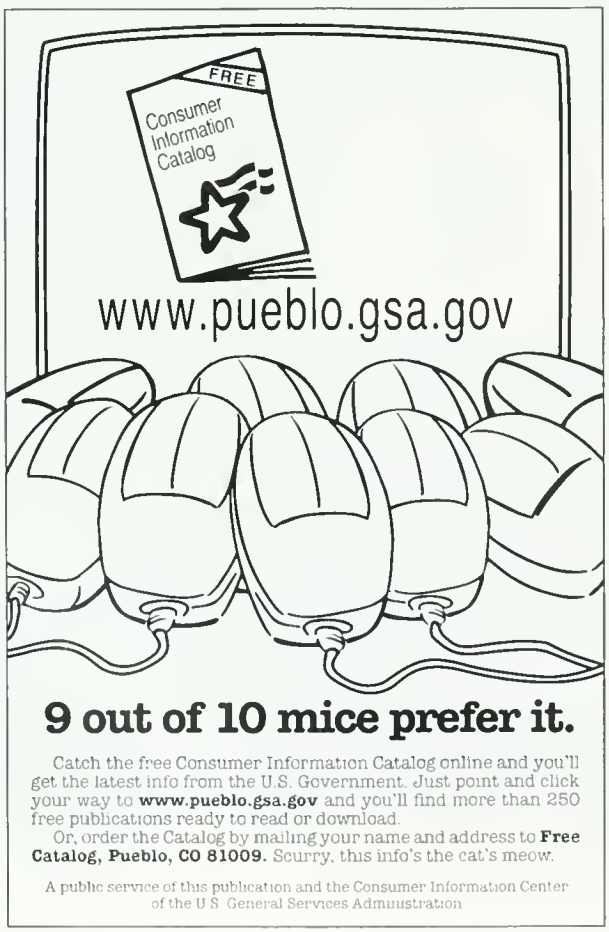
attributes), measured with the Health Utilities Index Mark 2 classification system, and health-related quality of life (utilities), quantified with 2-preference measurement techniques, were used to quantify each participant's self-reported, subjectively defined health state and 4 preselected hypothetical health states. RESULTS: Adolescents who were ELBW infants reported a higher number of attributes affected, as well as more complex and severe limitations in cognition, sensation, self-care, and pain, compared with controls. Statistically significant differences for the teenagers' health-related quality of life were noted between ELBW and control teenagers in the mean utility scores (0.87 ± 0.26 vs 0.93 ± 0.11; $p = 0.02$ on a conventional scale where 0 = dead and 1.00 = perfect health). However, a similar percentage of ELBW and control teenagers (71% vs 73%) gave utility ratings of more than 0.95 for their health status. CONCLUSIONS: Direct measures of self-reported health status and utility scores indicated that, as a cohort, adolescents who were ELBW infants suffer from a greater burden of morbidity and rate their health-related quality of life as significantly lower than control teenagers. Nevertheless, the vast majority of ELBW respondents view their health-related quality of life as quite satisfactory and are difficult to distinguish from controls. *See the related editorial:* ***Progress in Assessing the Long-Term Outcome of Extremely Low-Birthweight Infants****—JE Tyson, RS Broyles. JAMA 1996;276(6):492-493.*

Physician-Ordered Respiratory Care vs Physician-Ordered Use of a Respiratory Therapy Consult Service: Results of a Prospective Observational Study—JK Stoller, CI Skibinski, DK Giles, EL Kester, DJ Haney. Chest 1996;110 (2):422.

OBJECTIVE: To assess the impact of a respiratory therapy consult service (RTCS) on practices and appropriateness of ordering respiratory care services. DESIGN: Nonrandomized prospective observational cohort study with concurrent controls. SETTING: Adult non-ICU inpatient wards of an academic medical center. PATIENTS: A convenience sample of 98 adult non-ICU inpatients at the Cleveland Clinic Hospital, representing 20 inpatient clinical services. Patients whose respiratory care plans were determined by respiratory care practitioners using sign and symptom-based algorithms to specify treatment comprised the treatment group (n = 51, respiratory therapy consult group). The nonconsult group (n = 47) were patients whose respiratory care plans were specified by their own physicians. INTERVENTION: Specification of the respiratory care plan by the RTCS vs by the physicians themselves. Use of the RTCS was at the discretion of the managing physician. OUTCOME MEASURES: Types and number of respiratory care treatments, length of hospital stay, costs of the respiratory therapy provided, appropriateness of respiratory care orders (based on comparison of the actual respiratory care orders with a reference respiratory care plan generated by a study investigator who was kept blind to the actual respiratory care plan), and adverse respiratory events. RESULTS: Patients for whom the RTCS was requested by their physicians had a greater severity of respiratory illness based on having a lower triage score, but were otherwise similar at baseline. Fewer initial orders for respiratory care were discordant with the reference algorithms in RTCS patients (15% $\pm$ 26% [SD]) than in nonconsult patients (43% $\pm$ 36%; $p < 0.001$), and a smaller fraction of RTCS patients received at least 1 discordant initial respiratory care order (37% vs 72%; $p < 0.001$). Though provided to sicker patients with longer lengths of hospital stay, RTCS-directed care incurred similar respiratory care costs per patient ($335.63 $\pm$ $272.69 [RTCS] vs $349.06 $\pm$ $273.27; $p = 0.72$). CONCLUSIONS: These results sug-



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gest that the RTCS can be an effective strategy to allocate respiratory care strategies appropriately while conserving the costs of providing respiratory care. *See the related editorial:* ***Protocol-Driven Respiratory Therapy: Closing in on Appropriate Utilization at Comparable Cost and Patient Outcomes—KG Torrington. Chest 1996; 110(2):313-314.***

Ambulatory Visits to Hospital Emergency Departments: Patterns and Reasons for Use—GP Young, MB Wagner, AL Kellermann, J Ellis, D Bouley, for the 24 Hours in the ED Study Group. JAMA 1996;276(6):460.

OBJECTIVES: To characterize the reasons ambulatory patients use hospital emergency departments (EDs) for outpatient care and to determine the proportion of ED patients who initially are assessed as having nonurgent conditions, but subsequently are hospitalized. DESIGN: Cross-sectional survey during a single 24-hour period of time. SETTING: Fifty-six hospital EDs nationwide. PATIENTS OR OTHER PARTICIPANTS: Consecutive ambulatory patients presenting for care. Patients who arrived by ambulance were excluded. RESULTS: Of 6,441 ambulatory patients (79% of all ED visits) who were eligible for study, interviews were obtained from 6,187 (96%). A total of 5,323 patients (86%) had clinical reasons or preferences for seeking care at an ED, including 2,799 (45%) who thought they had an emergency or an urgent condition or were too sick to go elsewhere. Nineteen percent (n = 1,199) reported that they were sent to the ED by a health-care professional. Patients with a regular clinician or with insurance cited similar reasons for seeking care at an ED. A total of 3,062 patients (50%) cited 1 or more nonfinancial barriers to care as an important reason for coming to the ED, and 949 (15%) cited financial considerations. A total of 3,045 patients (49% of ambulatory patients and 37% of total ED visits) were assessed at triage as having a nonurgent condition; 166 of them (5.5%; 95% confidence interval, 4.7%-6.3%) were admitted to the hospital. CONCLUSIONS: Most ambulatory patients seek care in an ED because of worrisome symptoms or nonfinancial barriers to care. Although many ambulatory patients appear to have nonurgent conditions based on triage classification, a small but disturbing percentage of nonurgent patients are hospitalized. *See the related editorial:* ***Triage of Ambulatory Patients*** *—SL Adams, PB Fontanarosa. JAMA 1996;276(6):493-494.*

Pressures Required To Move Gas through the Native Airway in the Presence of a Fenestrated vs a Nonfenestrated Tracheostomy Tube—JD Hussey, MJ Bishop. Chest 1996;110(2):494.

SUBJECT: It is occasionally desirable for patients with a tracheostomy tube to breathe through their native airway. We hypothesized that capped tracheostomy tubes with cuffs deflated would create substantial additional resistance to airflow without fenestration but would provide minimal resistance to airflow when the tube had a fenestration. METHODS: Two tracheal models were tested simulating a large (26 mm) and an average (18 mm) trachea. Tests were carried out with fenestrated and nonfenestrated tracheostomy tubes of sizes ranging from No. 4 to No. 10. Negative pressure inspiration was simulated using suction. RESULTS: With a large trachea or small tubes, the suction required to generate flows of 40 L/min or greater remained < 5 cm H_2O with or without a fenestration. However, with an average-sized trachea and no fenestration, the pressure required to generate flows of 40 L/min or greater exceeded 5 cm H_2O and with No. 8 or No. 10 tubes exceeded 20 cm H_2O. A fenestration routinely reduced the required pressure to < 5 cm H_2O. CONCLUSION: The effort required to move gas across the native airway in the absence of a fenestration may be substantial. If a patient is to breathe through a native airway, a fenestrated tube should be used unless the tracheostomy tube is a No. 4.

Neonatal Mortality and Length of Newborn Hospital Stay—SA Beebe, JR Britton, HL Britton, P Fan, B Jepson. Pediatrics 1996;98(2):231.

BACKGROUND: To investigate the effect of hospital discharge time on neonatal mortality of term newborns. DESIGN: Infants who were discharged home at 5 days of age or younger and who subsequently died were compared with control infants using a retrospective case-control test. Descriptive information was collected from records of infants who were not discharged home from the hospital of birth (because of death or transfer to a tertiary care hospital) to determine the age at which their illnesses presented. METHODS: We reviewed death certificates for all infants with birthweights of 2,500 g or greater born at 37 weeks' gestational age or greater who died in the first 28 days of life and who were born in 1 of 4 Utah counties (1985 through 1989). Of the 109,256 eligible births, 115 infants were found who had died in the neonatal period. Eighty-four infants had not been discharged home from the hospital of birth, 5 infants had hospital stays of more than 5 days, 9 records could not be located, 17 presumed healthy infants were discharged from the hospital at 5 days of age or younger. These 17 infants were each matched with 3 control infants. Newborn nursery charts were reviewed to determine hospital discharge times for case and control infants. Descriptive information regarding the time of presentation of illness was collected for the other 89 infants. RESULTS: The mean age of hospital discharge was 43 ± 21 hours for the 17 case infants and 47 ± 25 hours for the 51 control infants. The odds ratio for neonatal mortality for discharge at less than 24 hours was 1.65 (95% confidence interval, 0.42 to 3.34) and for discharge at < 48 hours was 1.16 (95% confidence interval, 0.4 to 3.34). Of the 84 infants who were not discharged home from the hospital of birth, 93% had been symptomatic by 12 hours of age, and 99% were symptomatic by 18 hours. CONCLUSIONS: Most full-term infants who die in the neonatal period are symptomatic within the first 18 hours after birth. We could not demonstrate an association between early hospital discharge and neonatal mortality in those infants who died after discharge home.

Predicting the Duration of Mechanical Ventilation: The Importance of Disease and Patient Characteristics—MG Seneff, JE Zimmerman, WA Knaus, DP Wagner, EA Draper. Chest 1996; 110(2):469.

OBJECTIVE: To analyze the determinants of an individual patient's duration of mechanical ventilation and assess interhospital variations for average durations or ventilation. DESIGN: Prospective, multicenter, inception, cohort study. SETTING: Forty-two ICUs at 40 U.S. hospitals. PATIENTS: A total of 5,915 patients undergoing mechanical ventilation on ICU Day 1 selected from the acute physiology and chronic health evaluation (APACHE) III database of 17,440 admissions. INTERVENTIONS: None. MEASUREMENTS & RESULTS: Utilizing APACHE III data collected on the 5,915 patients, multivariate regression analysis was performed on selected patients and disease characteristics to determine which variables were significantly associated with the duration of mechanical ventilation. An equation predicting duration of ventilation was then developed using the significant predictor variables and its accuracy was evaluated. Variables significantly associated with duration of ventilation included primary reason for ICU admission, Day 1 acute physiology score (APS) of APACHE III, age, prior patient location and hospital length of stay, activity limits due to respiratory disease, serum albumin, respiratory rate, and P_{aO_2}/F_{IO_2} measurements. Using an equation derived from these variables, predicted durations of ventilation were then calculated and compared with actual observed durations for each of the 42 ICUs. Average duration of ventilation for the 42 ICUs ranged from 2.6 to 7.9 days, but 60% of this variation was accounted for by the differences in patient characteristics. CONCLUSIONS: For patients admitted to the ICU and ventilated on Day 1, total duration of ventilation is primarily determined by admitting diagnosis and degree of physiologic derangement as measured by APS. An equation developed using multivariate regression techniques can accurately predict average duration of ventilation for groups of ICU patients, and we believe this equation will be useful for comparing ventilator practices between ICU's, controlling for patient differences in clinical trials of new therapies or weaning techniques, and as a quality improvement mechanism.

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Adjusting FVC for the Effect of Obstruction—JJ Lefante, HW Glindmeyer, H Weill, RN Jones. Chest 1996;110(2):417.

OBJECTIVE: To derive a method of taking into account the effects of obstruction on the FVC, allowing more accurate assessment of other negative ("restrictive") influences. DESIGN: In 656 subjects with airways obstruction, defined as FEV_1/FVC of 0.70 or less, regression of FVC was expressed as percentage of predicted value (FVC %PRED) on potential explanatory variables, including FEV_1/FVC. The resulting equation was used to adjust FVC %PRED in 530 other obstructed men, to test whether the adjustment resulted in a different relationship of FVC %PRED to body weight. SETTING: A large occupational respiratory surveillance program utilizing rigorously quality-assured and standardized spirometry. SUBJECTS: The study included 5,188 men aged 45 to 65 years who denied fibrogenic dust exposures, including 656 with airways obstruction. RESULTS: There was a significant ($p < 0.0001$) linear relationship between more severe obstruction (lower FEV_1/FVC) and lower FVC %PRED. Depending on which of several predictive equations is used, obstruction explains 15 to 17% of variability in FVC %PRED over the entire range of severity of obstruction. Adjusting for obstruction in the separate group of 530 subjects showed a significantly larger effect of body weight on FVC %PRED. CONCLUSION: A simple equation can be used to discount the negative effects of obstruction on FVC. This allows more accurate clinical interpretation and can be useful in the analysis of epidemiologic data.

Clinical Strategies To Reduce Utilization of Chest Physiotherapy without Compromising Patient Care—E Alexander, S Weingarten, Z Mohsenifar. Chest 1996;110(2):430.

BACKGROUND: There is widespread interest in the evaluation of clinical strategies that safely reduce health-care costs. Elimination of inappropriate chest physiotherapy may represent one of those strategies. SETTING: An academic community hospital. METHODS: One-hundred one patients receiving chest physiotherapy were prospectively randomized to continue their chest physiotherapy or to inform their physicians that the order for the chest physiotherapy may have been inappropriate. RESULTS: Patients who were randomized to have their chest physiotherapy discontinued received 45% fewer chest physiotherapy treatments than control patients ($p < 0.01$). There was no increase in the mortality rate or length of hospital stay associated with the reduction in chest physiotherapy in carefully selected patients. The estimated cost savings would be $319,000, which is 50 times greater than the cost associated with the intervention. CONCLUSION: Chest physiotherapy is frequently provided to patients for inappropriate indications. Reducing chest physiotherapy for these patients may significantly reduce respiratory therapy costs without increasing length of stay or mortality rates.

The 6-Minute Walk Test Predicts Peak Oxygen Uptake and Survival in Patients with Advanced Heart Failure—LP Cahalin, MA Mathier, MJ Semigran, GW Dec, TG DiSalvo. Chest 1996;110(2):325.

BACKGROUND: The 6-minute walk test (6'WT) is a simple measure of functional capacity and predicts survival in patients with moderate heart failure (HF). METHODS: To assess the role of the 6'WT in the evaluation of patients with advanced HF, 45 patients (age 49 ± 8 years, mean ±SD; New York Heart Association class 3.3 ± 0.6; left ventricular ejection fraction 0.20 ± 0.06; right ventricular ejection fraction 0.31 ± 0.11) underwent symptom-limited cardiopulmonary exercise testing and the 6'WT during cardiac transplant evaluation. RESULTS: Mean 6'WT distance ambulated was 310 ± 100 m and peak oxygen uptake (peak $\dot{V}_{O_2}$) was 12.2 ± 4.5 mL/kg/min. There was a significant correlation between 6'WT distance ambulated and peak $\dot{V}_{O_2}$ ($r = 0.64$, $p < 0.001$). Multivariate analysis of patient characteristics, resting hemodynamics, and 6'WT results identified the distance ambulated during the 6'WT as the strongest predictor of peak $\dot{V}_{O_2}$ ($p < 0.001$). 6'WT distance ambulated less than 300 m predicted an increased likelihood of death or pretransplant hospital admission for continuous inotropic or mechanical support within 6 months ($p = 0.04$), but did not predict long-term overall or event-free survival with a mean follow-up of 62 weeks. Peak $\dot{V}_{O_2}$ was the best predictor of long-term overall and event-free survival. CONCLUSIONS: In patients with advanced HF evaluated for cardiac transplantation, distance ambulated during the 6'WT predicts (1) peak $\dot{V}_{O_2}$ and (2) short-term event-free survival. *See the related editorial:* ***Predicting Prognosis in Advanced Heart Failure****—MR Mehra, CJ Lavie, RV Milani. Chest 1996;110(2):310-312.*

Medication Nebulizer Performance: Effects of Diluent Volume, Nebulizer Flow, and Nebulizer Brand—D Hess, D Fisher, P Williams, S Pooler, RM Kacmarek. Chest 1996;110(2):498.

BACKGROUND: Medication nebulizers are commonly used to deliver aerosolized medications to patients with respiratory disease. We evaluated output and respirable aerosol available to the patient (inhaled mass) for 17 medication nebulizers using a spontaneous breathing lung model. METHODS: Three nebulizer fill volumes (3, 4, and 5 mL containing 2.5 mg of albuterol) and 3 oxygen flows (6, 8, and 10 L/min) were evaluated using the 17 nebulizers. A cotton plug at the nebulizer mouthpiece was used to trap aerosol during simulated spontaneous breathing. Following each trial, the amount of albuterol remaining in the nebulizer and the amount deposited in the cotton plug were determined spectrophotometrically. Aerosol particle size was determined using an 11-stage cascade impactor. RESULTS: Increasing fill volume decreased the amount of albuterol trapped in the dead volume ($p < 0.001$) and increased the amount delivered to the patient ($p < 0.001$). Increasing flow increased the mass output of particles in the respirable range of 1 to 5 μm ($p = 0.004$), but the respirable mass delivered to the patient was affected to a greater extent by nebulizer brand ($p < 0.001$) than flow. Although 2.5 mg of albuterol was placed into the nebulizers, less than 0.5 mg in the respirable range of 1 to 5 μm was delivered to the mouthpiece. CONCLUSIONS: The performance of medication nebulizers is affected by fill volume, flow, and nebulizer brand. When they are used for research applications, the nebulizer characteristics must be evaluated and reported for the conditions used in the investigation. *See the related editorial:* ***Aerosolized Drug Delivery in the 90s****—GC Smaldone. Chest 1996;110(2):316-317.*

Changes in the Inflammatory Response of the Lung during Acute Respiratory Distress Syndrome: Prognostic Indicators—RP Baughman, KL Gunther, MC Rashkin, DA Keeton, EN Pattishall. Am J Respir Crit Care Med 1996;154(1):76.

We studied paired bronchoalveolar lavage (BAL) in patients with sepsis-associated acute respiratory distress syndrome (ARDS). Patients were evaluated at 1 institution and underwent bronchoscopy with BAL within 48 hours of the onset of ARDS. Patients were restudied with bronchoscopy and BAL after 4 days of treatment. Fifty-eight patients were initially studied, with 44 patients having follow-up bronchoscopy after 4 days. The overall 30-day survival for the ARDS group was 60%. In the initial lavage, there was no difference in the neutrophils between the survivors and nonsurvivors (survivors: 59 [0-98]%; Median [Range]; nonsurvivors: 55 [0-92]%). The follow-up lavage demonstrated a significant drop in the neutrophils for the survivors (36 [4-89]%, $p < 0.002$) which was not seen for the nonsurvivors (70 [26-95]%). Initial IL-8 concentrations in the BAL fluid were not significantly different between the 2 groups. In the follow-up lavage, there was a significant fall for the IL-8 concentrations for the survivors but not the nonsurvivors. We conclude that neutrophil influx in ARDS may rapidly resolve within a week of the onset of ARDS. The resolution of neutrophils was associated with a good prognosis.

Effect of Ventilator-Associated Pneumonia on Mortality and Morbidity—L Papazian, F Bregeon, X Thirion, R Gregoire, P Saux, JP Denis, G Perin, J Charrel, JF Dumon, JP Affray, F Gouin. Am J Respir Crit Care Med 1996;154(1):91.

The aim of this study was to evaluate the attributable mortality and excess intensive care

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unit (ICU) stay as linked to ventilator-associated pneumonia (VAP) in a medical-surgical ICU. We performed a matched cohort study. The diagnosis of VAP was established when clinical, biologic, and radiologic signs of VAP were associated with the presence of at least 1 microorganism at a concentration $\geq 10^3$ CFU/mL on the protected specimen brush sample. Each case patient with VAP was matched to 1 control patient on the basis of the following potential confounding factors: same diagnosis and same indication for mechanical ventilation, same age ± 5 years, same sex, same APACHE II score ± 5 on admission. In addition, control patients had to be ventilated for at least as long as the case patient prior to the onset of VAP, and date of admission of the case and control patients had to be matched within 1 year. In 85 of the 97 patients with VAP, we were able to match 1 case patient with 1 control patient. Mortality was similar in both case (40%) and control (38.8%) patients. The duration of mechanical ventilation was increased in survivor case patients (27.2 ± 24.7 d) compared with survivor control patients (18.5 ± 15.7 d) ($p < 0.01$). The duration of hospitalization in ICU was increased in survivor case patients (34.9 ± 23.6 d) compared with survivor control patients (26.1 ± 18.6 d) ($p < 0.02$). When confounding factors were controlled, VAP did not appear to increase mortality.

Pneumonia in Intubated Patients: Role of Respiratory Airway Care—J Rello, R Soñora, P Jubert, A Artigas, M Rué, J Vallés. Am J Respir Crit Care Med 1996;154(1):111.

In order to assess potential risk factors for pneumonia within the first 8 days of ventilation, we studied 83 consecutive intubated patients undergoing continuous aspiration of subglottic secretions (CASS). Multivariate analysis showed the protective effect of antibiotic use (relative risk [RR] = 0.10; 95% confidence interval [CI] = 0.01 to 0.71), whereas failure of the CASS technique (RR = 5.29; 95% CI = 1.24 to 22.64) was associated with a greater risk of pneumonia. In addition, there was a trend toward a higher risk of pneumonia (RR = 2.57; 95% CI = 0.78 to 8.03) among patients with persistent intracuff pressures below 20 cm H_2O. The remaining factors analyzed were not significant. Failure of CASS did not influence the development of pneumonia among patients undergoing antibiotic treatment (33.0% vs 38.5%, $p > 0.20$), but was strongly associated with pneumonia (42.1% vs 8.3%, $p < 0.01$) among intubated patients not receiving antibiotics. When multivariate analysis was repeated in this subpopulation, failure of CASS (RR = 7.52, 95% CI = 1.48 to 38.07) and persistent intracuff pressure below 20 cm H_2O (RR = 4.23, 95% CI = 1.12 to 15.92) were factors independently associated with the development of pneumonia. We conclude that leakage of colonized subglottic secretions around the cuff of the endotracheal tube is the most important risk factor for pneumonia within the first 8 days of intubation. This study confirms the importance of maintaining adequate intracuff pressure and effective aspiration of subglottic secretions in preventing pneumonia in intubated patients not receiving antibiotic treatment.

Mortality of Nosocomial Pneumonia in Ventilated Patients: Influence of Diagnostic Tools—JF Timsit, S Chevret, J Valcke, B Misset, B Renaud, FW Goldstein, P Vaury, J Carlet. Am J Respir Crit Care Med 1996;154(1):116.

The over-mortality induced by nosocomial infections, especially pneumonia in ventilated patients (VNP), is still a matter of controversy because it is difficult to know precisely the respective effects of VNP per se and both the underlying illness and the severity of the disease that indicates ICU stay. During a 3-year period, for each patient mechanically ventilated for more than 48 hours we recorded underlying illness, reason for mechanical ventilation, clinical and therapeutic data collected during the first 48 hours of ventilation, and death in the ICU. Patients with suspicion of VNP (S-VNP) according to clinical, radiologic, and biologic criteria underwent bronchoscopy with protected specimen brush (PSB) and bronchoalveolar lavage culture (BAL-C). VNP was confirmed (C-VNP) if PSB $\geq 10^3$ cfu/mL and/or BAL-C $\geq 10^4$ cfu/mL. Prognostic multivariate analysis was performed introducing S-VNP and C-VNP as time-dependent covariates. Of the 387 studied patients, 112 S-VNP and 56 C-VNP were observed with overall mortality of 43% (168 patients). MacCabe, APACHE II score, shock, use of sedatives, and absence of enteral nutrition were additively associated with an increased mortality as well as C-VNP (relative risk [RR]: 1.8, $p = 0.007$). Nevertheless, when S-VNP and C-VNP were simultaneously introduced in the Cox model, only S-VNP remained associated with increased mortality. In patients suspected of VNP, confirmation of VNP using PSB and/or BAL-C adds no prognostic information. Whether this could be explained by the lack of sensitivity of protected distal samples or the severity of underlying conditions of S-VNP patients is still an open issue. A multivariate analysis based on follow-up data during the ICU course of ventilated patients will be initiated in the near future.

Noninvasive Capnometry in a Pediatric Population with Respiratory Emergencies—TJ Abramo, RA Wiebe, SM Scott, PA Primm, D McIntyre, T Mydler. Pediatr Emerg Care 1996;12(4):252.

OBJECTIVE: This study was designed to investigate the reliability, safety, and efficacy of measuring end-tidal CO_2 (ET_{CO_2}) in nonintubated pediatric patients presenting to an emergency department (ED) with respiratory emergencies. DESIGN/SETTING/PATIENTS: Eighty-five children were enrolled in a clinical, prospective, observational study at a university-affiliated children's hospital. Children age 4 weeks to 15.3 years with upper and lower respiratory diseases were enrolled by convenience sampling over a 5-month period. INTERVENTIONS: ET_{CO_2} measurements were obtained on each patient by oral/nasal sidestream capnometry. When a consistent waveform was obtained, the value was compared with a capillary arterial partial pressure of CO_2 (Cap_{CO_2}), oxygen saturation (O_{2Sat}), and clinical observations. RESULTS: Study patients had a mean ET_{CO_2} reading of 33 mm Hg with a standard deviation (SD) of 4.6 mm Hg and Cap_{CO_2} reading of 36 mm Hg with a SD of 4.5 mm Hg. Pulmonary findings, final diagnosis, and age did not significantly alter the relationship between Cap_{CO_2} and ET_{CO_2}. The relationship between Cap_{CO_2} and ET_{CO_2} was significant ($t = 14.9$, $p < 0.0001$, $r = 0.87$), with a 95% confidence interval for prediction of ± 5 mm Hg. CONCLUSION: Dependable ET_{CO_2} values can be obtained using an oral/nasal capnometry circuit, and they consistently correlate with Cap_{CO_2} in a pediatric population with upper and lower respiratory diseases. Noninvasive ET_{CO_2} analysis is safe and reliable within the limitations of this study group. Further exploration is necessary to determine the value of this technology in assisting with clinical decisions in the patient with impending respiratory failure.

Initial End-Tidal CO_2 Is Markedly Elevated during Cardiopulmonary Resuscitation after Asphyxial Cardiac Arrest—RA Berg, C Henry, CW Otto, AB Sanders, KB Kern, RW Hilwig, GA Ewy. Pediatr Emerg Care 1996;12(4):245.

OBJECTIVES: To compare the initial end-tidal CO_2 (Pet_{CO_2}) during cardiopulmonary resuscitation in asphyxial versus ventricular fibrillatory cardiac arrest. DESIGN: A cohort study. SETTING: University research laboratory. SUBJECTS: Forty domestic piglets. INTERVENTIONS: Asphyxial cardiac arrest was produced by clamping the endotracheal tube in 20 piglets and was continued for 10 minutes after loss of aortic pulsations occurred. Ventricular fibrillation (VF) was induced by applying 60 Hz of alternating current via a pacing wire to the myocardium of the other 20 piglets, and continued for a 15-minute downtime. Cardiopulmonary resuscitation (CPR) was then provided to each group for 2 minutes, followed by standard advanced cardiac life support protocols. MEASUREMENTS & MAIN RESULTS: All piglets were instrumented for continuous monitoring of Pet_{CO_2}, electrocardiogram, central venous pressure, and aortic pressure. Pet_{CO_2} of the first breath of CPR was 91 ± 20 mm Hg in the asphyxial group versus 34 ± 14 mm Hg in the VF group ($p < 0.001$). The asphyxial group continued to exhibit significantly greater Pet_{CO_2} for the first 5 breaths of resuscitation, after which there were no differences. The coronary perfusion pressures during the first breaths of CPR did not differ between the 2 groups. High initial Pet_{CO_2} did not

correlate with return of spontaneous circulation. CONCLUSIONS: End-tidal CO_2 during the first 5 breaths of CPR is much higher after an asphyxial cardiac arrest than VF. In each case, the initial Pet_{CO2} appears to reflect alveolar CO_2 prior to CPR. After 1 minute of CPR, Pet_{CO2} is useful in monitoring the effectiveness of CPR.

Alterations of End-Tidal Carbon Dioxide during the Intrahospital Transport of Children—JD Tobias, A Lynch, J Garrett. Pediatr Emerg Care 1996;12(4):249.

OBJECTIVE: To determine the effect of manual ventilation during intrahospital transport on end-tidal carbon dioxide concentrations in children. DESIGN: Prospective study in children who required tracheal intubation and mechanical ventilation/hyperventilation to maintain an arterial partial pressure of CO_2 (P_{aCO_2}) of 25 to 30 torr for control of intracranial pressure. SETTING: Pediatric intensive care unit. INTERVENTION: During patient transport with manual ventilation, end-tidal CO_2 was monitored with a side-streaming aspirating, infrared device. The person responsible for manual ventilation was informed of the current ventilator settings and the need to maintain a P_{aCO_2} of 25 to 30 torr, but was not allowed to see the end-tidal CO_2 monitor. RESULTS: The study population included 12 patients ranging in age from 7 months to 14 years (average age 6.9 years) and in weight from 6.5 to 57 kg (average weight 28.9 kg). A total of 1,716 end-tidal CO_2 values were recorded during 286 minutes of monitoring. Five hundred and thirty-one (31%) of the readings were in the intended range of 25 to 30 torr. Four hundred (23%) were < 20 torr, 665 (39%) were in the 20 to 24 torr range, and 119 (6.3%) were > 30 torr. Only five were > 40 torr. CONCLUSIONS: Unintentional hyperventilation occurs during the intrahospital transport of children. End-tidal CO_2 values < 25 torr were noted 62% of the time.

Delivery of Albuterol in a Pediatric Emergency Department—JR Williams, JP Bothner, RD Swanton. Pediatr Emerg Care 1996;12(4):263.

OBJECTIVE: To determine if albuterol delivery by the combination of a metered dose inhaler (MDI) with a spacer is equal in effectiveness to nebulization in a pediatric emergency department setting. DESIGN: Prospective series. SETTING: Urban children's hospital emergency department. PARTICIPANTS: Patients ≥ 6 years of age with the diagnosis of acute asthma exacerbation. Exclusion criteria consisted of impending respiratory failure and corticosteroid administration within the preceding 7 days. INTERVENTIONS: Patients were randomized into either the nebulizer treatment group or 1 of 2 MDI-spacer treatment groups (2 spacers were evaluated). Each patient received 3 albuterol treatments administered evenly over 1 hour. The dose ratio for albuterol by nebulizer versus MDI-spacer was 6.9:1. Outcome was assessed by comparing the pre- and posttreatment percent predicted respiratory rate and percent predicted peak expiratory flow rate (PEFR) for each patient. RESULTS: Sixty patients were enrolled in the study. All 3 treatment groups showed significant improvement following albuterol therapy in both percent predicted respiratory rate and percent predicted PEFR. When comparing the 3 groups against each other in regard to outcome, no significant differences were found in improvement of percent predicted respiratory rate ($p = 0.3258$) or percent predicted PEFR ($p = 0.9362$). CONCLUSIONS: In a pediatric emergency department setting, aerosolized albuterol delivered by MDI-spacer was equal in effectiveness to nebulization in the acute asthma management of children ≥ 6 years of age.

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Family Member Presence during Pediatric Emergency Department Procedures—A Sacchetti, R Lichenstein, CA Carraccio, RH Harris. Pediatr Emerg Care 1996;12(4):268.

OBJECTIVE: Exclusion of family members (FM) during pediatric procedures in the emergency department (ED) is an accepted practice. This study questions the validity of such a practice. SUBJECTS: FM of ED pediatric patients undergoing procedures and ED staff performing procedures. SITES: ED of a tertiary care university-affiliated community hospital and the pediatric ED of a university hospital. METHODS: Postprocedure surveys were obtained from FM remaining with their child during an ED procedure and from the ED personnel performing the procedures. FM activity during the procedure was also recorded. RESULTS: Ninety-six children (average age 20 months) underwent a total of 127 procedures. ED procedures included: vascular access 91, lumbar puncture 23, urethral catheterization 9, nasogastric tube placement 1, rapid sequence intubation 1, fluid resuscitation from shock 1, and removal of foreign body from eye 1. Three children were critically ill during performance of procedures. ED staff answered 98 surveys concerning the performance of the 127 procedures. FM ACTIVITIES INCLUDED: Stood at bedside 35 (31%), soothed child 21 (19%), and helped restrain child 55 (55%). In 55 (57%) cases the FM was the only adult present with the ED staff member performing the procedure(s). FM OPINIONS OF PRESENCE DURING PROCEDURES WERE: Good idea 101 (91%), bad idea 6 (5%), and did not care 4 (4%). ED staff opinions were: good idea 92 (93%), bad idea 2 (2%), and did not care 4 (5%). FM presence made 4 (5%) members of the ED staff nervous. CONCLUSION: FM presence during ED procedures is a practice favored by both parents and ED staff at our institutions. This practice should not be limited to minimally invasive procedures in stable patients but should be considered for procedures such as lumbar punctures and intubations even in critically ill patients.

Prediction of Childhood Drowning and Near-Drowning Morbidity and Mortality—DM Habib, FW Tecklenburg, SA Webb, NG Anas, RM Perkin. Pediatr Emerg Care 1996;12(4):255.

OBJECTIVES: (a) Evaluate the presenting hemodynamic status and neurologic function of a series of warm water submersion injuries. (b) To ascertain the importance of the timing of the neurologic examination. (c) To identify risk factors that predict which patients will not return to presubmersion status. DESIGN: Retrospective review of all patients with a diagnosis drowning/near-drowning responded to by the Children's Hospital pediatric transport service. Data were collected over a 24-month period regarding patient characteristics, submersion medium, rescue efforts, time out of sight, elapsed times to emergency department (ED) and pediatric intensive care unit (PICU) arrival, neurologic and hemodynamic status on arrival at the ED and PICU, reconstructed Conn-Modell category, and neurologic outcome. SETTING: EDs of the referring hospitals and PICU of the Children's Hospital of Orange County (CHOC), California. PATIENTS: Ninety-three submersion victims at an average age of 31 months. All patients were provided intensive care support. INTERVENTION: None. MEASUREMENTS & MAIN RESULTS: Twenty-three percent (21/93) of patients died or survived vegetative. No patient arriving comatose and asystolic in the ED survived neurologically intact (n = 21, 3 patients expired in the ED). This group of patients had a mean duration of documented asystole = 41 minutes, range of 18 to 107 minutes, and time to ED arrival = 21 minutes. All patients with a detectable pulse and blood pressure (n = 72) on arrival to the ED, regardless of their neurologic status, recovered to their presubmersion status. Patients arriving comatose (decorticate, decerebrate, or flaccid posture) in the PICU (n = 18, mean arrival = 192 minutes) all died or were vegetative. All patients with non-coma (n = 72, Conn-Modell category A or B) on arrival to the PICU recovered normally. CONCLUSIONS: Hemodynamic status in the ED and neurologic status in the PICU are highly predictive of outcome. On arrival to the ED, the cardiovascular status is more predictive of abnormal outcome than neurologic status. Poor neurologic outcome appears inevitable for warm water submersion victims who are asystolic at ED arrival and remain comatose for more than 200 minutes.

Calf's Lung Surfactant Extract in Acute Hypoxemic Respiratory Failure in Children—DF Willson, JH Jiao, LA Bauman, A Zaritsky, H Craft, K Dockery, D Conrad, H Dalton. Crit Care Med 1996;24(8):1316.

OBJECTIVE: Open-label trial of the safety and short-term efficacy of calf's lung surfactant in pediatric respiratory failure. DESIGN: Multi-institutional, uncontrolled, observational trial. SETTING: Six pediatric intensive care units of tertiary medical centers. PATIENTS: Twenty-nine children with acute hypoxemic respiratory failure, characterized by diffuse, bilateral, pulmonary infiltrates, need for ventilator support, and an oxygenation index of ≥ 7. INTERVENTIONS: Up to 4 doses of intratracheal surfactant (80 mL/m^2). MEASUREMENTS & MAIN RESULTS: Ventilator parameters, arterial blood gases, and derived oxygenation and ventilation indices were recorded before, and at intervals after, surfactant administration. Complications and outcome measures were also noted. There was immediate improvement in oxygenation and moderation of ventilator support associated with surfactant administration in 24 of 29 patients. A modest but statistically insignificant effect was seen with subsequent doses. The only complications occurred in 3 patients who developed airleaks, two of which were coincident with surfactant administration. The overall mortality rate was 14%, which compares favorably with other published series. CONCLUSIONS: Administration of calf's lung surfactant appears to be safe and is associated with rapid improvement in oxygenation and moderation of ventilator support in children with acute hypoxemic respiratory failure. These results set the stage for a randomized, controlled study.

State Tobacco Lobbyists and Organizations in the United States: Crossed Lines—AO Goldstein, NS Bearman. Am J Public Health 1996;86(8):1137.

OBJECTIVES: This research took a quantitative look at state-level tobacco lobbying in the United States. METHODS: Publicly available lobbying data were collected from all states during 1994. Data were compiled on tobacco industry lobbyists, their tobacco employers, health lobbyists, and factors associated with such lobbying. RESULTS: In 1994, 450 tobacco industry lobbyists lobbied at a state level. Most lobbying was on behalf of 4 organizations: Philip Morris (34%), the Tobacco Institute (21%), RJ Reynolds (17%), and the Smokeless Tobacco Council (15%). Approximately one half of all tobacco lobbyists also lobbied for a health-related organization (eg, state medical association, hospital, physician association). CONCLUSIONS: All U.S. states have tobacco lobbyists. Many health organizations knowingly or unknowingly employ lobbyists who also lobby for the tobacco industry.

Cerebral Oxygenation Monitoring by Near-Infrared Spectroscopy Is Not Clinically Useful in Patients with Severe Closed-Head Injury: A Comparison with Jugular Venous Bulb Oximetry—SB Lewis, JA Myburgh, EL Thornton, PL Reilly. Crit Care Med 1996;24(8):1334.

OBJECTIVE: To compare continuous jugular venous bulb oximetry and cerebral near-infrared spectroscopy in patients with severe closed head injury. DESIGN: A prospective observational study. SETTING: Intensive care unit of a major teaching hospital. PATIENTS: Adults (n = 10) with severe closed-head injury (Glasgow Coma Scale score of ≤ 8). INTERVENTIONS: None. MEASUREMENTS & MAIN RESULTS: Jugular venous bulb oximetry, cerebral near-infrared spectroscopy, and cerebral perfusion pressure were measured continuously. A total of 3,691 paired measurements of near-infrared spectroscopy and jugular venous bulb oximetry were analyzed. Poor correlation ($r^2 = 0.04$) between paired measurements and wide limits of agreement (−13% to +21%) were demonstrated. The mean difference between measurements was ± 4% and the standard deviation of the mean difference was +8.69%. The data were subsequently grouped according to 3 clinically significant subgroups of jugular venous bulb oxygen saturation reflecting low

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(< 55%), normal (55% to 75%) and high (> 75%) saturation values. Poor correlation and wide limits of agreement between the 2 methods of measurement were observed in all groups. Values recorded by near-infrared spectroscopy did not significantly change between the groups, and 14 clinically significant episodes of jugular venous bulb desaturation were not detected by near-infrared spectroscopy. CONCLUSIONS: Tissue oxygen saturation determined by near-infrared spectroscopy does not reflect significant changes in cerebral oxygenation detected by the global measurement of jugular venous bulb oximetry. This finding may be explained by inadequate signal detection and inaccuracies in the algorithm used to filter out extracranial components. Until these technical difficulties are addressed, near-infrared spectroscopy, as measured by the machine assessed in this study, cannot be routinely recommended for assessment of cerebral oxygenation in patients with acute head injury.

Positive End-Expiratory Pressure-Induced Hemodynamic Changes Are Reflected in the Arterial Pressure Waveform—R Pizov, M Cohen, Y Weiss, E Segal, S Cotev, A Perel. Crit Care Med 1996;24(8):1381.

OBJECTIVE: To examine whether the hemodynamic changes due to mechanical ventilation with positive end-expiratory pressure (PEEP) can be assessed by the respiratory-induced variations in the arterial pressure waveform during normovolemia and experimental acute ventricular failure. DESIGN: Prospective, controlled experimental study. SETTING: Institutional experimental laboratory. SUBJECTS: Adult mongrel dogs. INTERVENTIONS: Experimental acute ventricular failure was induced by the infusion of pentobarbital (a cardiodepressant) and methoxamine (a vasoconstrictor), combined with volume loading. Both the control and acute ventricular failure groups were subjected to ventilation with incremental levels of PEEP up to 20 cm H_2O. MEASUREMENTS & MAIN RESULTS: Cardiac function was evaluated by cardiac output and left and right ventricular change in pressure over time (dP/dt) measurements. Arterial pressure waveform analysis was performed by measuring the systolic pressure variation, which is the difference between the maximal and minimal systolic blood pressure values during 1 mechanical breath. The components of the systolic pressure variation, namely, dUp and dDown, which are the increase and decrease in the systolic pressure during the mechanical breath relative to the systolic pressure during apnea, were also measured at each PEEP level. PEEP caused significant reduction of cardiac output in normovolemic dogs, and was associated with significant increases in systolic pressure variation and dDown. Acute ventricular failure decreased the variations in the systolic pressure and caused the dDown component to disappear. The application of PEEP did not affect cardiac output in dogs with acute ventricular failure, nor did it change systolic pressure variation and the dDown. CONCLUSIONS: Analysis of arterial pressure waveforms during mechanical ventilation reflected the decrease in cardiac output in dogs with normal cardiac function subjected to incremental PEEP. In dogs with acute ventricular failure in which PEEP did not affect cardiac output, the systolic pressure variation was similarly unaffected by PEEP. In the absence of cardiac output measurement during mechanical ventilation with PEEP, the analysis of the respiratory variations in the arterial pressure waveform may be useful in assessing changes in cardiac output.

Predicting Outcome in Children with Severe Acute Respiratory Failure Treated with High-Frequency Ventilation—AP Sarnaik, KL Meert, MD Pappas, PM Simpson, MW Lieh-Lai, SM Heidemann. Crit Care Med 1996;24(8):1396.

OBJECTIVES: (a) To demonstrate the effect of high-frequency ventilation on gas exchange in children with severe acute respiratory failure unresponsive to conventional ventilation; (b) to identify patients at high risk of death early after institution of high-frequency ventilation. SETTING: Tertiary care pediatric intensive care unit in a university hospital. DESIGN: A cross-sectional, observational study with factorial design. PATIENTS: Thirty-one patients with severe acute respiratory failure defined as a P_{aO_2}/F_{IO_2} of < 150 torr (< 20 kPa) with a positive end-expiratory pressure of ≥ 8 cm H_2O and/or P_{aCO_2} of > 60 torr (> 8 kPa) with an arterial pH < 7.25. INTERVENTIONS: Patients received either high-frequency oscillation or jet ventilation if respiratory failure was unresponsive to conventional ventilation and if the underlying disease process was deemed reversible. MEASUREMENTS & MAIN RESULTS: Thirty-one children were managed with high-frequency ventilation, 11 children with jet and 20 children with oscillator. Arterial blood gases and level of ventilatory support were recorded before and at 6, 24, 48, 72, and 96 hours after institution of high-frequency ventilation. There was an improvement in an arterial pH, P_{aCO_2}, P_{aO_2}, and P_{aO_2}/F_{IO_2} 6 hours after institution of high-frequency ventilation ($p < 0.01$). This improvement, along with decreased need for oxygen, was sustained through the subsequent course. Twenty-three (74%) of 31 children treated with high-frequency ventilation survived. Survivors showed an increase in an arterial pH, P_{aO_2}, P_{aO_2}/F_{IO_2}, and a decrease in P_{aCO_2} within 6 hours, whereas nonsurvivors did not. Oxygenation index was the best predictor of outcome. A combination of an initial oxygenation index of > 20 and failure to decrease the oxygenation index by > 20% by 6 hours after initiation of high-frequency ventilation predicted death with 88% (7/8) sensitivity and 83% (19/23) specificity, with an odds ratio of 33 ($p = 0.0036$, 95% confidence interval 3-365). CONCLUSIONS: In patients with potentially reversible underlying diseases resulting in severe acute respiratory failure that is unresponsive to conventional ventilation, high-frequency ventilation improves gas exchange in a rapid and sustained fashion. The magnitude of impaired oxygenation and its improvement after high-frequency ventilation can predict outcome within 6 hours.

Directly Observed Therapy for Tuberculosis: The Harlem Hospital Experience, 1993—W El-Sadr, F Medard, V Barthaud. Am J Public Health 1996;86(8):1146.

OBJECTIVES: A directly observed therapy program was established at Harlem Hospital, New York NY, in 1993 to promote high tuberculosis treatment completion rates. METHODS: The Harlem program used an on-site surrogate family model. Treatment completion rate, visit adherence rate, human immunodeficiency virus seroprevalence, and time of sputum culture conversion were assessed. RESULTS: Out of 145 enrolled patients with suspected and confirmed tuberculosis, 95 (92 confirmed and 3 suspected) continued treatment. The visit adherence rate was 91.1 ± 7.9%, with 1 patient (1%) lost to follow-up. CONCLUSION: High rates of treatment completion and visit adherence were achieved because of unique program characteristics. Thus, directly observed therapy is advocated as a means of ensuring treatment completion.

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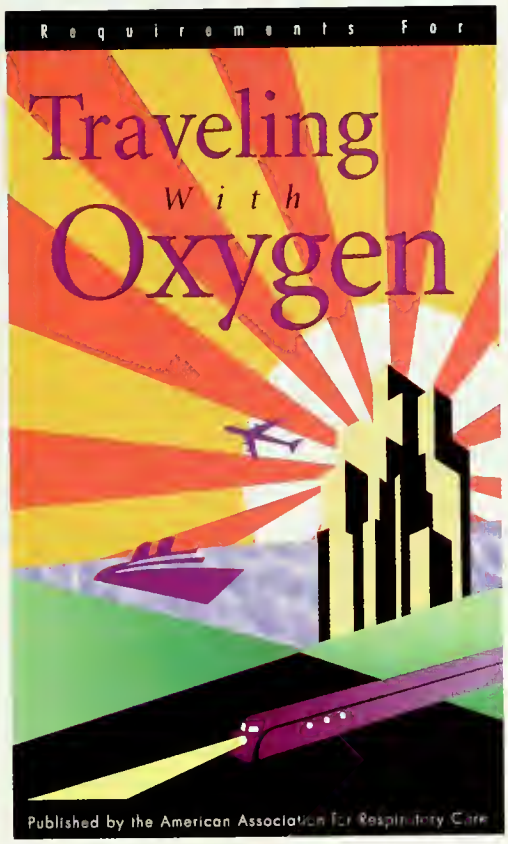

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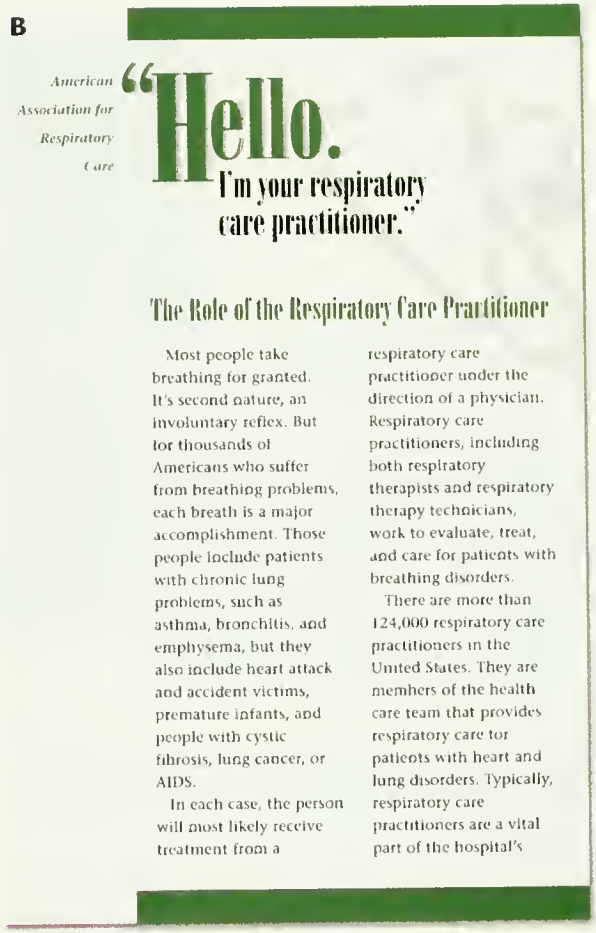
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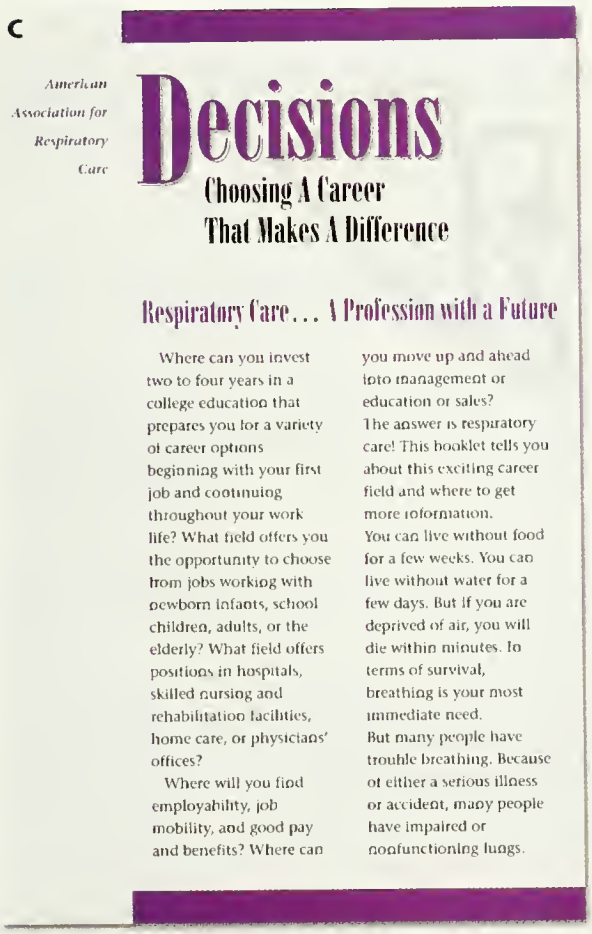
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Comparison of Aerosol Delivery via Circulaire Nebulizer System versus a Disposable Nebulizer in COPD Patients

John W Mason RRT and Warren C Miller MD

BACKGROUND: In this study, we compared aerosol deposition from the Circulaire Nebulizer System (CS) to deposition from a conventional disposable nebulizer in COPD patients and assessed the physiologic response to bronchodilator aerosol with these devices. EVALUATION METHODS & PATIENT SELECTION: In a prospective randomized, crossover-controlled study of 10 patients with COPD by history and objective testing, we compared the CS to a conventional nebulizer by quantitative radioaerosol scanning, pulmonary function testing, and pulse monitoring. RESULTS: The CS performed better in terms of reduction of side effects (total obliteration of mean pulse increase), extrapulmonary body deposition (5-fold reduction), and environmental contamination (3-fold reduction). Equal bronchodilatation and pulmonary deposition were achieved. Compared to normal subjects, COPD patients receive less lung dose of bronchodilator aerosol with either device. CONCLUSIONS: For usual bronchodilator treatment, the CS provides equal therapeutic effect with relative freedom from side effects and less exposure for caregivers. [Respir Care 1996;41(11):1006-1008]

Background

When the Circulaire Nebulizer System (CS)* was being introduced to clinical use, we studied its aerosol deposition characteristics in normal subjects compared to those of a conventional small volume nebulizer.[1] We demonstrated improved efficiency of aerosol delivery to the lungs, reduced aerosol deposition in the body outside of the lungs, and less escape of aerosol to the surroundings. The logical extension of these findings to the clinical environment would be improved therapeutic response, fewer side effects, and less risk to caregivers, but studies in normal subjects do not necessarily reflect the results found in sick patients. Therefore, we asked What is the aerosol deposition of these devices in chronic obstructive pulmonary disease (COPD) patients, frequent recipients of such therapy? Moreover, the inclusion of patients in these studies introduces abnormal physiology and the opportunity to directly study therapeutic response and side effects.

Evaluation Methods & Patient Selection

The details of our methods for quantitative aerosol scanning have been reported previously.[1,2] A small measured amount of radioactive technetium is added to the solution to be nebulized, and following aerosol administration the patient is scanned with a gamma camera. Correction is made for attenuation, washout, and isotope decay. Regions of interest are counted including pharynx-esophagus-stomach (extrapulmonary deposition, ie, gastrointestinal deposition, or % GI), and lung (pulmonary deposition, % Lungs). In addition, the expiratory filter is scanned and counted to assess environmental contamination (% Room). To measure the depth of aerosol

The authors are associated with the Respiratory Section, Columbia Clear Lake Regional Medical Center, Webster, Texas.

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Mr Mason has no financial interest in these products; Dr Miller is a consultant for WestMed Inc.

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penetration into the lungs, the outer half of the lung by area is compared to the inner half; and, the measurement is expressed as the ratio of those areas, or the penetration index (PI). The baseline area is the area revealed by radioactive xenon scan performed on each patient before the study began.

Following approval of the study by our Institutional Review Board, we recruited 10 outpatients with COPD as reflected by history and spirometric results, who were in a clinically stable state with no recent hospitalizations or changes in therapy or symptoms. Each gave informed consent for participation in the study. Patient demographics are depicted in Table 1. Each subject was permitted to continue usual activities and therapy except that bronchodilator aerosols were proscribed for 4 hours prior to the study. Each patient was studied on 2 separate days, 1 with the conventional nebulizer, and 1 with the CS. No change in therapeutic programs occurred between the 2 study days. The order of study was randomized by coin toss. Spirometry in accordance with standards of the American Thoracic Society[3] was performed before and 5-10 minutes after aerosol treatments on each study day. All studies were scheduled at 2:00 PM. To the nebulizers were added a unit dose of albuterol solution (2.5 mg in 3.0-mL volume) and approximately 3 millicuries of radioactive 99m technetium diethylenetriamine-penta acetate in 0.5-mL volume. Consistent with common clinical practice, nebulization was continuous (without the use of an airflow finger valve) and proceeded to 'dryness' with sputtering and no further production of visible aerosol. Pulse rates were monitored with a pulse oximeter. Statistical analysis was by the *t* test for paired variables.

Table 1. Characteristics of the 10 Patients Included in the Study Comparing 2 Nebulizers

Patient	Age (years)	Gender	FEV_1* (% predicted)	FEV_1/FVC
1	68	M	43	0.44
2	68	F	46	0.56
3	71	F	82	0.69
4	75	M	63	0.65
5	67	M	43	0.48
6	70	F	58	0.56
7	60	M	35	0.44
8	63	F	61	0.44
9	68	F	47	0.44
10	72	F	28	0.64
Mean (SD)	68 (4)	—	51(16)	0.53 (0.10)

*FEV_1 = forced expiratory volume in the first second of expiration, expressed as percent of predicted normal, and FEV_1/FVC = the ratio of FEV_1 to forced vital capacity, both measured at baseline on the day of conventional nebulization.

Results

Composite data are depicted in Table 2. No statistically significant differences were seen between the baseline pulmonary function on either day or in the degree of bronchodilatation achieved with treatment by the 2 nebulizers. Extrapulmonary deposition was reduced 5-fold by the CS ($p < 0.001$). The tachycardia induced by bronchodilator therapy was virtually absent with the CS ($p < 0.01$ level). Environmental contamination was reduced 3-fold ($p < 0.01$). Although the CS appeared to deposit slightly more in the lungs, the results were not significantly different from the conventional nebulizer. In a similar way, no significant difference was seen in the penetration index.

Discussion

The results obtained in the aerosol-deposition portion of this study in COPD patients is similar to our results in normal subjects. Compared to the conventional nebulizer studied, CS appears to deliver about the same amount of aerosol to the lung. (The difference was not statistically significant.) Both extrapulmonary deposition in the body and environmental contamination were significantly reduced with the CS. In clinical practice, reduced environmental contamination should reduce the inadvertent inhalation of aerosol by caregivers, but we have not specifically studied caregiver risk. We have not rigorously proven that the deposition of radioactive particles is identical to the deposition of active bronchodilator drug and do not claim that correspondence between deposition and physiologic studies is exact. Nevertheless, considering our study group as a whole, similar lung deposition was related to similar change in pulmonary function, and reduced extrapulmonary deposition was related to obliteration of the pulse increase often observed. This suggests equivalent therapeutic effect with relative freedom from side effects with the CS.

The penetration indices we measured in these patients were lower than those we observed in normal subjects. Although this in part reflects the actual penetration, it is in part due to baseline artifact in that the projected area of the baseline xenon scan taken at functional residual capacity in COPD patients is usually larger than in normal subjects of comparable size because of the hyperinflation and air trapping seen in COPD patients.

Despite smaller aerosol particles and what appeared to be more homogeneous scans with the CS, we were unable to demonstrate a better depth of penetration of aerosol into the lungs. We have considered that this finding might be an artifact of our study. However, we use an imaging technique, and others using similar techniques for studying other nebulizers have found similar results.[4] Imaging techniques have also been used in the study of metered dose inhalers (with and without spacers) with similar findings in bronchitic patients.[5] In asthmatics, imaging techniques failed to show penetration differences with aerosolization of inhaled steroids.[6] Another approach to the evaluation of the level of penetration of the aerosol into the lung is the so-called functional technique, which assumes that inhaled radioactive particles remaining in the lung after 24 hours have been deposited deeply—beyond the

Table 2. Measures of Deposition and Clinical Response with Conventional (CN) and Circulaire (CS) Nebulizers

Patient	Pulse Change		FEV_1 (pre-BD*/post-BD)		% Lungs		Penetration Index		% GI		% Room	
	CN	CS	CN	CS	CN	CS	CN	CS	CN	CS	CN	CS
1	11	8	1.4/1.6	1.3/1.4	5.0	12.4	0.30	0.37	2.9	0.4	35	8
2	7	−8	1.0/1.0	1.0/1.0	4.4	4.5	0.61	0.52	7.6	1.3	29	20
3	34	7	1.8/2.1	2.0/2.2	8.3	7.8	0.47	0.52	2.9	1.1	36	12
4	8	−2	1.9/1.9	1.7/1.9	7.8	5.9	0.37	0.49	6.3	1.4	36	15
5	10	2	1.3/1.4	1.1/1.4	9.5	7.1	0.21	0.22	3.2	0.5	35	7
6	−4	1	1.0/1.1	1.1/1.3	3.7	2.1	0.41	0.32	10.3	1.4	30	6
7	20	−1	1.2/1.2	1.3/1.3	6.4	8.7	0.28	0.33	3.2	0.9	36	11
8	9	−2	1.3/1.4	1.2/1.4	5.3	5.7	0.24	0.33	7.0	1.7	31	10
9	8	−14	0.9/1.1	0.9/1.2	5.2	8.8	0.82	0.39	3.7	1.4	39	8
10	40	4	0.6/0.7	0.5/0.7	12.3	12.1	0.35	0.40	6.6	0.5	37	14
Mean	14	0	1.2/1.4	1.2/1.4	6.8	7.5	0.41	0.39	5.4	1.1	34	11
(SD)	(13)	(7)	(0.4/0.4)	(0.4/0.4)	(2.7)	(3.2)	(0.19)	(0.10)	(2.6)	(0.5)	(3)	(4)

*BD = bronchodilator; penetration index = ratio of radioactivity in outer lung area to radioactivity in inner lung area; GI = gastrointestinal.
Statistically significant at $p < 0.01$; $p \geq 0.05$ was considered not significant.

relatively rapid mucociliary clearance of the bronchi—and, hence, represent alveolar deposition. The functional technique has been used in several studies of metered dose inhalers with and without spacers with similarly unimproved penetration of the aerosol.[7-9] These results taken collectively suggest that aerosol methods of any sort have been ineffective in improving aerosol penetration.

With identical study techniques, we found less aerosol deposited in the lungs of these COPD patients compared to our normal subjects. There is other evidence that the amount of aerosol deposition in the lungs is inversely related to impairment in pulmonary function.[10] It appears that the patients most in need of aerosol actually receive the least. There is a rising body of opinion that trials of high dose aerosols may be beneficial;[11,12] and, we are studying the results of administering higher doses of aerosols.

In Conclusion

We believe that our results establish that the Circulaire Nebulizer System provides a therapeutic effect equal to that obtained with the comparison nebulizer, with relative freedom from side effects and less potential exposure to caregivers.

PRODUCT SOURCES

Nebulizers:
Airlife, Misty-Neb, Baxter HealthCare Corp, Valencia CA
Circulaire system, WestMed Inc, Tucson AZ

Testing Materials:
Radioactive technetium, Mallinckrodt Medical, St Louis MO
Gamma camera, GE Medical Systems, Milwaukee WI
Albuterol, generic product
Expiratory filter, generic product

Spirometer:
Model 2200, Sensormedics, Yorba Linda CA

REFERENCES

1. Mason JW, Miller WC, Small S. Comparison of aerosol delivery via Circulaire system vs conventional small volume nebulizer. Respir Care 1994;39(12):1157-1161.
2. Miller WC, Mason JW. Aerosol deposition of a propylene glycol solution. J Aerosol Med 1991;4(4)293-296.
3. American Thoracic Society. Standardization of spirometry—1994 update. Am J Respir Crit Care Med 1995;152(3):1107-1136.
4. Johnson MA, Newman SP, Bloom R, Talese N, Clark SW. Delivery of albuterol and ipratropium bromide from two nebulizer systems in chronic stable asthma. Efficacy and pulmonary deposition. Chest 1989;96(1):6-10.
5. Dolovich M, Ruffin R, Corr D, Newhouse MT. Clinical evaluation of a simple demand inhalation MDI aerosol delivery device. Chest 1983;84(1):36-41.
6. Kao CH, Lin HT, Yu SL, Wang SJ, Leu JL. Effects of corticosteroid inhalation therapy on the deposition pattern of Tc-99m human serum albumin radioaerosols in asthma. Lung 1995;173(5):291-296.
7. Newman SP, Moren F, Pavia D, Little F, Clarke SW. Deposition of pressurized suspension aerosols inhaled through extension devices. Am Rev Respir Dis 1981;124(3):317-320.
8. Newman SP, Millar AB, Lennard-Jones TR, Moren F, Clarke SW. Improvement of pressurised aerosol deposition with Nebuhaler spacer device. Thorax 1984;39(12):935-941.
9. Newman SP, Woodman G, Clarke SW, Sackner MA. Effect of InspirEase on the deposition of metered-dose aerosols in the human respiratory tract. Chest 1986;89(4):551-556.
10. Howatt JS, Gorvoy JD, Smaldone GC. Quantitative deposition of aerosolized gentamicin in cystic fibrosis. Am Rev Respir Dis 1987;136(6):1445-1449.
11. Lai CKW, Legge JS, Friend JAR. Air-driven nebulised high-dose salbutamol in severe chronic obstructive airways disease: is it safe? Respiration 1991;58(5-6):249-254.
12. Tashkin DP. Dosing strategies for bronchodilator aerosol delivery. Resp Care 1991;36(9):977-988.

Auto-PEEP Associated with Excessive Oxygen Flow through Five Manual Resuscitators

Charles W Reick Jr MS RRT

I undertook this study to confirm or invalidate my observation that health care providers use oxygen flows higher than recommended by the manufacturers of manual resuscitators and to explore possible clinical consequences associated with use of high flows. MATERIALS & METHODS: Part 1. A convenience sample of 7 Registered Respiratory Therapists (RRTs), 3 second-year respiratory therapy students who had completed the cardiopulmonary resuscitation component of their curriculum, 6 critical care registered nurses (CCRNs), 2 emergency room nurses, and 2 registered nurses who were instructors in Advanced Cardiac Life Support were instructed to set the oxygen flow to a Mercury CPR Bag equipped with an oxygen reservoir in a manner consistent with their normal practice. Flow output to the resuscitator was measured using a calibrated Timeter RT-200. Part 2. I evaluated the effect of high oxygen flow on the performance of 4 disposable and 1 nondisposable bag-valve manual resuscitator. An oxygen flow of 15 L/min was introduced to each manual resuscitator while the resuscitator was connected to the inlet port of a test lung set to simulate normal compliance and airway resistance. The 'lung' was ventilated at a rate of 12 breaths/min and a tidal volume of 0.7-0.8 L. Flow was increased in 5 L/min increments and auto-PEEP readings were taken, using the test lung's "Intra-Pulmonary" manometer. Test lung compliance was than reduced and the procedure repeated. The compliance was then returned to normal and the airway resistance increased. The procedure was repeated. RESULTS: Part 1. Flows averaged 36.9 L/min compared to recommended flows of 15 L/min. Part 2 showed that high oxygen flows may result in clinically important levels of auto-PEEP. Auto-PEEP appeared at flows as low as 35 L/min in one resuscitator and at flows of 55 L/min in all resuscitators under conditions of high airway resistance. CONCLUSIONS: Results suggest that even trained health care providers ignore or are unfamiliar with manufacturer recommendations. This disregard could have important clinical consequences. Stronger emphasis should be placed on the correct use of manual resuscitators in programs designed to prepare health care providers to provide assisted manual ventilation. [Respir Care 1996;41(11):1009-1012]

Introduction

Bag-valve manual resuscitators (so-called resuscitation bags) are often used to provide ventilation during cardiopulmonary resuscitation and during endotracheal suctioning and transport of patients who require ventilatory assistance. Many aspects of operator and resuscitator performance have been studied.[1-12] In many of these studies, the resuscitators were operated according to manufacturer specifications. In the 'real' world, I have observed that operators sometimes forget or ignore manufacturers' specifications when using manual resuscitators. I have observed the use of oxygen flows to manual resuscitators at levels higher than recommended by standard texts and manufacturers' specifications. Eubanks and Bone in *Principles and Applications of Cardiopulmonary Care Equipment* note

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that "the use of high oxygen flow rates (above 15 L/min) is not recommended [through bag-valve manual resuscitators] without a special attachment because it may interfere with the function of the valve in some units."[13] Similarly, Barnes, Schreuder, and Israel in *Respiratory Care Principles: A Programmed Guide to Entry-Level Practice* (3rd edition) write that "The oxygen flow to the resuscitator should always be at 15 L/min when ventilating adults, and it should always be higher than minute volume being delivered. ... It is absolutely incorrect to take an oxygen flowmeter to flush, since the flow can be as high as 50 L/min, which may lock the patient valve and cause high airway pressures."[14] In spite of such injunctions, I have observed that health care providers tend not to pay attention to flow settings. Flows are typically adjusted until the reservoir bag remains inflated during inspiration and/or until the resuscitator 'sounds right.' I sought to determine whether practitioners operate manual resuscitators at oxygen flows higher than those recommended by manufacturers and to explore the possible effects these high oxygen flows might have on resuscitator performance.

Materials & Methods

Part 1 of the study was designed to determine whether practitioners operate manual resuscitators at oxygen flows higher than those recommended by the manufacturer. A convenience sample of 7 Registered Respiratory Therapists (RRTs), 3 second-year respiratory therapy students who had completed the cardiopulmonary resuscitation component of their curriculum, 6 registered nurses in critical care (CCRNs), 2 emergency room nurses, and 2 registered nurses who were Advanced Cardiac Life Support (ACLS) instructors was recruited. Participants were instructed to set oxygen flow to a Mercury CPR Bag with oxygen reservoir* in a manner consistent with their normal practice. After flow was set, the flow output to the resuscitator was measured using a calibrated Timeter RT-200.

Part 2 of the study was designed to explore the effect of high oxygen flows on the performance of 4 disposable (Mercury CPR Bag, Baxter Safe Care, Ambu Spur, and Respironics BagEasy) and 1 nondisposable (Laerdal Silicone) bag-valve manual resuscitator. As a baseline, an oxygen flow of 15 L/min was introduced to each manual resuscitator while the resuscitators were connected to the inlet port of a calibrated Vent Aid TTL Training/Test Lung Model 1600. The compliance of the test lung was initially set to 0.05 L/cm H_2O and the resistance to approximately 2.48 cm $H_2O \cdot s \cdot L^{-1}$. Auto-PEEP was read as the end-expiratory 'intrapulmonary' pressure measured by the test lung and recorded at a respiratory rate of 12 and delivered tidal volume (V_T) of 0.7-0.8 L. Flow was increased in 5 L/min increments to a maximum of 85 L/min. Compliance of the test lung was then decreased to 0.02 L/cm H_2O and the procedure repeated. Compliance was then returned to 0.05 L/cm H_2O, and resistance was increased to approximately 24.59 cm $H_2O \cdot s \cdot L^{-1}$, and the procedure repeated.

*Suppliers of commercial products are listed in the Product Sources section at the end of the text.

Results

Oxygen flows set by practitioners were higher than those recommended by the manufacturers. Raw data are presented in Table 1. The average flow used by all practitioners was 36.95 L/min. The average maximum flow output from the Timeter flowmeters used in the study was 48 L/min (range, 46-51 L/min). The average flow selected by the respiratory care practitioners was 32 L/min; by the respiratory care students, 47.3 L/min; and by nurses, 37.3 L/min.

Table 1. Flows to Bag-Valve Manual Resuscitators Provided by 20 Health Care Providers

Practitioner	Flow Setting
Registered Respiratory Therapists	
1	44 L/min
2	30 L/min
3	32 L/min
4	38 L/min
5	28 L/min
6	36 L/min
7 (Clinical Instructor)	16 L/min
Respiratory Therapy Students	
1	49 L/min
2	47 L/min
3	46 L/min
Critical Care Registered Nurses	
1 (Surgical ICU*)	39 L/min
2 (Surgical ICU)	41 L/min
3 (Surgical ICU)	39 L/min
4 (Surgical ICU)	38 L/min
1 (Medical ICU)	26 L/min
2 (Medical ICU)	36 L/min
Emergency Room Registered Nurses	
1	39 L/min
2	38 L/min
Registered Nurses/Advanced Cardiac Life Support Instructors	
1	39 L/min
2	38 L/min

*ICU = Intensive Care Unit

Results of Part 2 demonstrated that high oxygen flows to manual resuscitators produce resistance to expiratory flow and can result in auto-PEEP. Table 2 shows the relationship between oxygen flow and auto-PEEP in a model simulating a patient with reasonably normal compliance and airway resistance. Auto-PEEP developed in 1 resuscitator (Baxter) at a flow of 40 L/min and in all resuscitators at flows of 65 L/min. At maximum flow, 85 L/min, the highest auto-PEEP level was found with the Baxter product, 10 cm H_2O, and the lowest level with

the Respironics and Laerdal, 4 cm H_2O. Reduced pulmonary compliance resulted in later appearance of auto-PEEP and overall lower auto-PEEP values, and increased airway resistance resulted in the earlier appearance of auto-PEEP and overall higher auto-PEEP values (Table 2).

Table 2. Auto-PEEP Associated with Oxygen Flows through 5 Manual Resuscitators

Oxygen Flow (L/min)	Manual Resuscitator Auto-PEEP (cm H_2O)				
	Ambu	Baxter	Respironics	Mercury	Laerdal
C_{TL} = 0.05 mL/cm H_2O, R_{TL} = 2.48 cm H_2O · s · L^{-1}, f = 12, V_T = 0.7 L					
15	0	0	0	0	0
20	0	0	0	0	0
25	0	0	0	0	0
30	0	0	0	0	0
35	0	0	0	0	0
40	0	1	0	0	0
45	0	3	0	3	0
50	2	4	0	3	1
55	4	5	0	3	2
60	5	6	0	4	2
65	6	7	2	5	3
70	6	8	3	5	3
75	7	9	4	6	3
80	8	10	4	6	4
85	9	10	4	6	4
C_{TL} = 0.02 mL/cm H_2O, R_{TL} = 2.48 cm H_2O · s · L^{-1}, f = 12, V_T = 0.7 L					
15	0	0	0	0	0
20	0	0	0	0	0
25	0	0	0	0	0
30	0	0	0	0	0
35	0	0	0	0	0
40	0	0	0	0	0
45	0	2	0	0	0
50	2	4	0	2	0
55	2	5	0	3	0
60	2	6	0	4	0
65	4	7	0	5	0
70	5	7	2	5	2
75	6	8	3	6	3
80	6	8	4	6	3
85	7	9	4	6	4
C_{TL} = 0.05 mL/cm H_2O, R_{TL} = 24.6 cm H_2O · s · L^{-1}, f = 12, V_T = 0.7 L					
15	0	0	0	0	0
20	0	0	0	0	0
25	0	0	0	0	0
30	0	0	0	2	0
35	0	2	0	4	0
40	2	3	0	5	0
45	3	5	0	5	1
50	3	6	0	6	3
55	3	8	1	11	4
60	4	9	2	11	4
65	4	10	3	14	4
70	4	10	4	14	4
75	4	12	4	18	4
80	4	13	4	18	4
85	4	13	4	18	4

Discussion

Although this study is descriptive in nature and limited both by the number of participants and the number of devices evaluated, I believe it demonstrates that even trained and experienced health care providers frequently ignore manufacturers' recommendations concerning the oxygen flow delivery to manual resuscitators and that disregarding these recommendations may have important clinical consequences.

To my knowledge, this is the first study to evaluate how health care providers in the hospital set oxygen flows to manual resuscitators. In a 1994 abstract by Branson et al, it was noted that care providers (physicians, nurses, respiratory therapists) "typically provided a higher f [respiratory rate] and lower V_T than suggested by AHA [American Heart Association] Standards" when ventilating patients in the emergency department.[15] It is, therefore, not surprising that practitioners might also deviate from other related standards when manually venting a patient.

This is also, to my knowledge, the first study to evaluate the effect of high oxygen flows on the performance of bag-valve manual resuscitators. A 1992 study by Hess and Simmons[12] demonstrated that significant differences existed in back pressures measured due to flow resistance through the patient valves of the 12 manual resuscitators they tested. They concluded that some of these pressures "might be excessive in some cases" and might prolong exhalation thereby predisposing the patient to auto-PEEP and its clinical consequences.[12] In this and similar studies,[11,16] a standard oxygen input flow of 15 L/min to the manual resuscitators was used, and expiratory resistance back pressure was measured while directing a flow of oxygen through the resuscitators' exhalation valves to simulate the expiratory flow from a patient. The exhalation valve was forced to vent the patient's exhaled gas plus any excess flow from the oxygen entering the resuscitator. In my study, the exhalation valve was the conduit for oxygen input flows many times that of the standard, manufacturer-recommended oxygen flows used in previous studies. This additional excess flow forces the 'patient's' exhaled gas to compete with the excessive oxygen input flow for egress through the exhalation valve; thus, when the pressure in the resuscitator bag exceeds the expiratory force of the patient, gas trapping and auto-PEEP occur.

This study shows that the high flows employed by care providers could result in clinically important levels of auto-PEEP in some of the devices evaluated. Auto-PEEP was found to rise as high as 18 cm H_2O. Even if we allow that the human lung is far more complex than a test lung, the implication of these bench results for clinical practice is that patients ventilated with manual resuscitators operated with oxygen flows above those specified by the manufacturer may be placed at risk for PEEP-related barotrauma and/or hypotension. The latter complication could have grave con-

sequences for the patient who presents with hypotension and/or requires cardiopulmonary resuscitation. Kollef[17] highlighted these consequences by describing a case of electromechanical dissociation and cardiogenic shock that resulted from the adverse effects of lung hyperinflation during manual ventilation.

Although I did not study such devices, the introduction of oxygen-conserving flow-metering devices with an on/off mode of operation may further complicate matters. These devices, designed to be used with manual resuscitators, provide a fixed flow (some set to 15 L/min, others at flush flow) when activated. Those configured for flush flow may have a flow output exceeding 80 L/min, far exceeding all recommended oxygen flow for manual resuscitators, and the routine use of flush-flow oxygen conservation devices should be questioned.

More sophisticated study of my findings and how they translate to clinical practice is indicated.

Conclusions

Stronger emphasis should be placed on the correct use of manual resuscitators in initial, remedial and 'refresher' programs designed to prepare health care personnel to provide manual ventilation.

PRODUCT SOURCES

Resuscitators:

CPR, Mercury Medical, Clearwater FL
Adult BagEasy, Respironics, Murrysville PA
SPUR, Ambu, Hanover MD
Adult Manual Resuscitator, Baxter, Deerfield IL
Silicone Adult Resuscitator, Laerdal, Armonk NY

Flowmeters:

0-75, Timeter, Lancaster PA
PM Eliminator, Precision Medical, Northampton PA

Calibration Analyzers:

RT-200, Timeter, Lancaster PA
Vet Aid TTI. Training/Test Lung, Dixie, Houston TX

REFERENCES

1. Hess D, Baran C. Ventilatory volumes using mouth-to-mouth, mouth-to-mask, and bag-valve-mask techniques. Am J Emerg Med 1985;3(4): 292-296.
2. Elling R, Politis J. An evaluation of emergency medical technicians ability to use manual ventilation devices. Ann Emerg Med 1983;12(12): 765-768.
3. Harrison RR, Maull KI, Keenan RL, Boyan CP. Mouth-to-mask ventilation: a superior method of rescue breathing. Ann Emerg Med 1982; 11(2):74-76.
4. Hess D, Goff G, Johnson K. The effect of hand size, resuscitator brand, and use of two hands on volumes delivered during adult bag-valve ventilation. Respir Care 1989;34(9):805-810.
5. Hess D, Goff G. The effect of two-hand versus one-hand ventilation on volumes delivered during bag-valve ventilation at various resistances and compliances. Respir Care 1987;32(11):1025-1028.
6. Jesudian MCS, Harrison R, Keenan RL, Maull KI. Bag-valve-mask ventilation—two rescuers are better than one: preliminary report. Crit Care Med 1985;13(2):122-123.
7. Hess D, Spahr C. An evaluation of volumes delivered by selected adult disposable resuscitators: the effect of hand size, number of hands used, and use of disposable medical gloves. Respir Care 1990;35(8): 800-805.
8. Barnes TA, Stockwell DL. Evaluation of ten manual resuscitators across an operational temperature range of −18° C to 50° C. Respir Care 1991;36(3):161-172.
9. Barnes TA, Potach R. Evaluation of five adult disposable operator-powered resuscitators. Respir Care 1989;34(4):254-261.
10. Barnes TA, McGarry WP III. Evaluation of ten disposable manual resuscitators. Respir Care 1990;35(10):960-968.
11. Mills PJ, Baptiste J, Preston J, Barnas GM. Manual resuscitators and spontaneous ventilation—an evaluation. Crit Care Med 1991;19(11): 1425-1431.
12. Hess D, Simmons M. An evaluation of the resistance to flow through the patient valves of twelve adult manual resuscitators. Respir Care 1992;37(5):432-438.
13. Eubanks D, Bone R. Principles and applications of cardiopulmonary care equipment. St Louis: Mosby, 1995.
14. Barnes TA, Schreuder JK, Israel JS. Respiratory care principles: a programmed guide to entry-level practice. 3rd ed. Philadelphia: Davis, 1995.
15. Branson R, Davis K Jr, Johnson R, Campbell R, Tabor T. Manual ventilation during cardiopulmonary resuscitation (abstract). Respir Care 1994;39(11):1068.
16. Barnes, TA. Evaluation of ten adult disposable manual resuscitators (abstract). Respir Care 1995;40(11):1192.
17. Kollef, M. Lung hyperinflation caused by inappropriate ventilation resulting in electromechanical dissociation: a case report. Heart Lung 1992;21(1):74-77.

Work of Breathing and Pressure-Time Product on Pressure Support Ventilation, Continuous Positive Airway Pressure, and T-Piece

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BACKGROUND: After prolonged mechanical ventilation (MV), weaning may include gradual unloading of respiratory muscles, followed by trials of CPAP or spontaneous breathing on a T-piece. We compared the total work of breathing (WOB) and pressure-time product (PTP) on mechanically ventilated patients during: (1) 5 cm H_2O of pressure support ventilation (PSV_5); (2) 5 cm H_2O CPAP using continuous-flow via an adjustable Downs flow generator (DFG) with an external PEEP valve ($CPAP_{CF-5}$); (3) 5 cm H_2O CPAP using the Siemens Servo 900C with a demand-valve system ($CPAP_{DV-5}$); and (4) T-piece. METHODS: Measurements of WOB and PTP were obtained in 23 medical patients deemed ready for liberation from MV by standard clinical criteria, who had been ventilated for respiratory failure of various etiologies. WOB and PTP determinations were made for 5-minute intervals with a CP-100 Pulmonary Monitor and then analyzed using a Gaussian-breath-elimination method to omit breaths with artifactual changes in esophageal pressure caused by swallowing, coughing, and other non-ventilatory maneuvers. RESULTS: All patients were successfully liberated from MV. WOB in J/L: PSV_5 = 0.89, $CPAP_{CF-5}$ = 0.98, $CPAP_{DV-5}$ = 0.99, and T-piece = 1.07. PTP in cm $H_2O \cdot s \cdot min^{-1}$: PSV_5, = 197, $CPAP_{CF-5}$ = 221, $CPAP_{DV-5}$ = 222, and T-piece = 228. By ANOVA, WOB was comparable among the various modes and T-piece (p = 0.77); similar results were obtained for PTPs (p = 0.74). CONCLUSION: Although the mechanism of maintaining positive airway pressure is different with PSV_5, $CPAP_{CF-5}$, and $CPAP_{DV-5}$, our study shows that the WOB and the PTPs are comparable with that of the T-piece, a spontaneous breathing mode. If the patient's ventilatory demands are met adequately, then low-level positive pressure and T-piece are equally effective for not developing respiratory muscle fatigue. Thus, following gradual weaning with PSV, when ventilatory demands are met and respiratory muscle performance is good, trials with T-piece or 5 cm H_2O of CPAP, instead of 5 cm H_2O of PSV on the Siemens Servo 900C, may offer no benefit prior to extubation or decannulation. To our knowledge, this is the only clinical study that demonstrates that at 5 cm H_2O, WOB and PTP on the Siemens Servo 900C in the CPAP mode are comparable to those of a continuous-flow CPAP system using an adjustable DFG with a non-reservoir circuit and an external PEEP valve. [Respir Care 1996;41(11):1013-1019]

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Introduction

Gradual weaning with pressure support ventilation (PSV) is considered to improve respiratory muscle strength and endurance in the mechanically ventilated patient recovering from prolonged acute respiratory failure.[1-4] Some physicians proceed with extubation or decannulation at a level of 5 cm

H_2O on PSV.[1,2] Others employ a trial of spontaneous breathing, either through a T-piece[2,3] or continuous positive airway pressure (CPAP) of 5 cm H_2O,[4] instead of 5-cm H_2O PSV to ensure adequate respiratory muscle performance.

Mechanisms affecting the work of breathing (WOB) are different with PSV and CPAP at a level of 5 cm H_2O. PSV provides partial ventilatory support by delivering a selected amount of positive pressure in response to a spontaneous inspiratory effort. Thus the ventilator assumes some inspiratory WOB. At low levels (5 cm to 8 cm H_2O), PSV has been shown to reduce the inspiratory work by overcoming the resistance of the endotracheal tube and the breathing circuit.[4,5] CPAP is a spontaneous ventilatory mode in which positive pressure is maintained throughout the breathing cycle. CPAP decreases inspiratory work by improving pulmonary mechanics,[6] offsetting intrinsic positive end-expiratory pressure (or auto-PEEP),[7] and improving gas exchange.[8]

CPAP can be delivered either by a continuous flow system or through a pressure-triggered or flow-triggered demand valve. Studies have shown that at a level of 5 cm H_2O on the Siemens Servo 900C, WOB on continuous flow CPAP is either comparable to[9-11] or lower than[12] WOB during pressure-triggered CPAP. Several studies have shown WOB on PSV to be lower than WOB on CPAP at 10 cm H_2O or higher inspiratory airway pressure.[13-16] However, there are few studies comparing PSV and CPAP at a level of 5 cm H_2O inspiratory airway pressure.[17,18] Using the measurement of total WOB, Lee et al[17] showed no difference among PSV of 5 cm H_2O, CPAP of 5 cm H_2O, and T-piece in 8 patients recovering from respiratory failure. Using the measurement of pressure-time product (PTP) in a group of 10 patients, 7 of whom had chronic obstructive pulmonary disease, Sassoon et al[18] found a difference between PSV of 5 cm H_2O, CPAP of 5 cm H_2O, and T-piece. Our objective was to determine whether WOB and PTP differ among PSV, CPAP, and T-piece in patients who are weaned gradually with PSV and ready to be extubated or decannulated. The total WOB and the PTP have gained wide acceptance for the evaluation of the respiratory muscle activity. Both indices are reliable predictors of weaning from mechanical ventilation.[1,18,19]

Methods

Subjects & Protocol

This study was approved by the University of Mississippi Investigation Review Board. The patient population consisted of 23 patients in the Medical Intensive Care Unit who initially required mechanical ventilation due to various etiologies (Table 1). At the time of the study, the acute process had resolved and the patients were being gradually weaned until they could tolerate PSV at a level of 5-10 cm H_2O with an

Table 1 Characteristics of Patients Studied

Patient No.	Age	Indication for MV*	I.D. of ET or TT (mm)	PNP (cm H_2O)	Duration of MV (days)
1	50	Intracranial bleed	8.5	60	25
2	28	Pneumonia; sepsis	9	30	15
3	36	Pneumonia; ethanol intoxication	8	60	6
4	40	Pneumonia; OSA; COPD	8.5	60	62
5	36	Exacerbation of bronchial asthma	8	60	8
6	61	DKA; severe renal failure	8.5	35	12
7	24	Pneumonia; sepsis; rhabdomyolysis	8	60	6
8	28	Ventricular fibrillation; severe renal failure	8.5	40	10
9	70	Pneumonia; COPD	8.5	35	8
10	84	Thromboembolic stroke	7.5	20	7
11	53	Pneumonia; OSA	8.5	80	15
12	66	Pneumonia; sepsis; status epilepticus	7	30	11
13	68	Respiratory arrest; UAO, pneumonia	9	30	20
14	18	Pneumonia; sepsis	8	60	25
15	27	Pneumonia; tracheal stenosis	7	55	5
16	20	Pneumonia; sepsis	8	45	11
17	58	Pneumonia; OSA	7	50	16
18	77	Pneumonia; myasthenia gravis	7	50	8
19	51	Pneumonia; postoperative CABG	8	20	13
20	45	Pneumonia; OSA	8	20	13
21	66	Pneumonia; postoperative CABG; mitral valvuloplasty	8.5	40	43
22	45	Pneumonia; DKA; myocardial infarction	8	30	8
23	66	Pneumonia; OSA; COPD	8.5	60	36

MV = mechanical ventilation, I.D. = internal diameter, ET = endotracheal tube; TT = tracheostomy tube, PNP = peak negative pressure; OSA = obstructive sleep apnea; COPD = chronic obstructive pulmonary disease; DKA = diabetic ketoacidosis, UAO = upper airway obstruction, CABG = coronary artery bypass graft.
* Indicates that TT was used.

external PEEP of 5 cm H_2O. Prior to data collection, the patients were rested overnight on assist control ventilation (ACV) using a Siemens Servo 900C.* After data collection, the patients were observed for at least 24 hours before liberation from mechanical ventilation.

According to the protocol, each patient breathed on (1) PSV of 5 cm H_2O and PEEP of zero cm H_2O with the Siemens Servo 900C ventilator (PSV_5); (2) CPAP of 5 cm H_2O from a demand valve with the Siemens Servo 900C ventilator ($CPAP_{DV-5}$); (3) continuous-flow CPAP of 5 cm H_2O ($CPAP_{CF-5}$); and (4) T-piece. Continuous-flow CPAP was provided by an adjustable Downs flow generator (DFG), a disposable, corrugated plastic tube, a non-reservoir humidified circuit, and an external PEEP valve. The continuous flow delivered by the DFG was set at approximately 75 L/min but could be adjusted to meet patient peak inspiratory flow by maintaining constant positive airway pressure if necessary. The T-piece apparatus consisted of an inspiratory limb, T-piece, and an expiratory limb. The inspiratory limb consisted of a disposable, corrugated plastic tube, approximately 72 inches long, which provided an air-oxygen mixture from an entrainment nebulizer. With an adequate oxygen flow (10-12 L/min) and F_{IO_2} of 0.30-0.40, inspiratory gas flow up to 60 L/min could be achieved. The expiratory limb consisted of a disposable, corrugated plastic tube, approximately 12 inches long, to prevent entrainment of room air. Adequate inspiratory flow was judged by observing the nebulizer mist escaping from the expiratory limb, particularly paying attention to early inspiration when inspiratory flow was maximal.

Modes were sequenced pseudorandomly (by computer generated numbers); before and after each mode the patient was rested on ACV. The patient stabilized for a period of 20-30 minutes during the new ventilatory mode before data were collected for 5 minutes. Each patient was tested in a semirecumbent position. Trigger sensitivity was set at −2 cm H_2O and working pressure was maintained at 70 cm H_2O on the Siemens Servo 900C ventilator during PSV and CPAP modes. A humidified F_{IO_2} of 0.30-0.40 was maintained constant in all modes. A pass-over heated humidifier was used during PSV_5, $CPAP_{DV-5}$, and $CPAP_{CF-5}$ modes. All patients were clinically stable at the time of the study, and all were successfully liberated from mechanical ventilation. The pulmonary fellow and attending physician made all clinical decisions regarding care and liberation from mechanical ventilation without knowing the study results or receiving input from the investigators.

Data Collection & Analysis

The WOB per unit volume (J/L), and PTP (cm $H_2O \cdot s \cdot min^{-1}$) were measured using a CP-100 Pulmonary Monitor. The flow transducer, used for continuous measurements of airway flow and airway pressure, was placed at the proximal end of the endotracheal or tracheostomy tube in mechanically ventilated patients. Esophageal pressure was measured with an esophageal balloon added to a nasogastric tube. Balloon placement was checked in each patient by using the airway occlusion test.[20]

Data were sent from the pulmonary monitor to a personal computer (PC) via a serial port and stored in the PC using software provided by Bicore. The monitor calculates the WOB and PTP by measuring esophageal pressure, airway pressure, and flow.

Patient work of breathing is an integration of the negative esophageal pressure during inspiration times flow plus chest-wall work divided by tidal volume to normalize the value.

$$WOB = (P_{ee} - P_{es})\, d\dot{V} + \frac{V_p^2}{2\, C_{cw}} ,$$

where P_{ee} = end-expiratory esophageal pressure; P_{es} = esophageal pressure at the beginning of the breath; $d\dot{V}$ = flow; V_p = patient portion of tidal volume; and C_{cw} = chest-wall compliance (assumed at 200 mL/cm H_2O).

PTP is measured as the integral of esophageal pressure and time for the duration of contraction of the respiratory muscles.

$$PTP = \left[(P_{ee} - P_{es}) + \frac{V_T}{C_{cw}}\right] \frac{dt}{t_{min}} ,$$

where P_{ee} = end esophageal pressure; P_{es} = current esophageal pressure; V_T = current tidal volume; C_{cw} = chest-wall compliance (assumed at 200 mL/cm H_2O); dt = sample time; and t_{min} = duration of breath in minutes.

The WOB in J/min was calculated breath by breath by our data analysis program by multiplying WOB per unit volume by the minute ventilation. Data in the PC were analyzed using a Gaussian-breath-elimination method that we developed[21] in order to omit breaths with artifactual changes in esophageal pressure due to non-respiratory maneuvers. Esophageal pressure swings unassociated with inspiration are common in ventilated patients (associated with swallowing, motility, and coughing). Such pressure swings can cause an erroneous increase in measured WOB, erroneous because it represents the work of swallowing or coughing, not the true work of inspiring. In measuring WOB breath by breath, it is difficult to objectively eliminate data when coughing occurs; furthermore, swallowing and esophageal motility are not readily apparent even at the bedside. However, because these pressure swings are more marked than those associated with ventilation, we found that they can be objectively distinguished from true breaths. A universal cutoff point cannot be used because pressures vary among patients, depend on the ventilatory modes, and are affected by superimposed pressures,

*Suppliers of commercial products are listed in the Product Sources section at the end of the text.

for example, when CPAP is used. The difference between the change in esophageal pressure during a breath, and the change in airway pressure during the same breath remains relatively constant during breathing in the same patient on the same mode. This difference, however, varies quite a bit during non-breathing maneuvers. During the course of a given data collection period (5 minutes in this study), the breath-by-breath difference can be fitted with a Gaussian distribution, as we would expect because the breaths should be normally distributed. The differences from the non-breathing maneuvers, however, do not fall in the normal distribution. We obtain the mean and standard deviation from the fit of the Gaussian curve (which are different than the mean and standard deviation of the data points). We then consider a point to be from a non-breathing maneuver if its difference falls outside 2 standard deviations from the mean of the Gaussian fit. These points are eliminated from further analysis. This process is totally automated and thus objective. Its validity has been checked in normal volunteers who were made to cough, swallow, and breathe against an occlusion, and, as a negative control, to breathe at twice the respiratory frequency (WOB J/L shouldn't change and didn't), and in patients who were coughing.[21]

Statistical Analysis

One-way analysis of variance (ANOVA) was used to test the hypothesis that WOB is equal among PSV_5, $CPAP_{CF}$, $CPAP_{DV}$, and T-piece. PTP was similarly tested. Results were considered significant at a $p < 0.05$. Prior to the study initiation, power analysis was performed to calculate sample size. Using ANOVA with 4 modes of ventilation, a $p < 0.05$, the usually accepted Power of 80%, and a variation of 0.2 J/L, we determined that a sample size of approximately 20 was sufficient to allow us to detect a 20% difference in WOB among the various groups. A variation of 0.2 J/L is the usual variation we find in WOB; a 20% difference was chosen because such a change is clinically important. Although previous studies have used a 50% difference, in our experience a 20% change in WOB would cause us to change our clinical management of a patient.

Results

The age of the patients, initial indication of mechanical ventilation, size of the endotracheal tube or tracheotomy tube, peak negative pressure and duration of mechanical ventilation are listed in Table 1.

The mean results for WOB per unit volume (J/L), WOB per minute (J/min), and PTP (cm $H_2O \cdot s \cdot min^{-1}$) during PSV_5, $CPAP_{CF-5}$, $CPAP_{DV-5}$, and T-piece are shown in Table 2. The mean WOB and PTP among the various groups were comparable and showed less than a 20% difference; they were not statistically different.

The mean values for tidal volume, respiratory rate, auto-PEEP, effective dynamic compliance, duty cycle, and rapid shallow breathing index during the different modes are shown in Table 3. There were no statistical differences among any of these variables.

Discussion

This study found no significant differences in total WOB with PSV_5, $CPAP_{CF-5}$, $CPAP_{DV-5}$, and T-piece in patients who required prolonged mechanical ventilation. Our study supports the preliminary data of Lee and co-workers,[17] who found no difference in total WOB with PSV_5, $CPAP_{DV-5}$, and T-piece in 8 patients recovering from respiratory failure. They were all mechanically ventilated with a Siemens Servo 900C. Their absolute WOB was much higher than that in the current study and probably reflects the time at which the data were obtained.

The PTP is measured at the beginning of respiratory muscle contraction when there is no flow; thus, it includes isometric work done to overcome auto-PEEP and to trigger the ventilator for the delivery of gas flow. The measurement of PTP differs from that of total WOB because the measurement of PTP includes both isometric and volumetric work of breathing and has been shown to correlate better with the oxygen consumption by the respiratory muscle than does total WOB.[22] In our group of patients, PTP on PSV_5, $CPAP_{CF-5}$, $CPAP_{DV-5}$, and T-piece showed no difference. This is in contrast to the findings of Sassoon et al in a group of 10 patients success-

Table 2. Sample with Standard Deviation and Standard Error of the Estimate for Work of Breathing (WOB) and Pressure Time Product (PTP) among Various Modes in 23 Patients

	PSV_5*	$CPAP_{DV-5}$	$CPAP_{CF-5}$	T-Piece	p Value
WOB (J/L)	0.89 (0.56, 0.12)	0.98 (0.54, 0.11)	0.99 (0.56, 0.12)	1.07 (0.62, 0.13)	0.77
WOB (J/min)	9.03 (5.88, 1.23)	10.22 (6.25, 1.30)	8.67 (5.10, 1.06)	9.54 (5.09, 1.06)	0.80
PTP (cm $H_2O \cdot s \cdot min^{-1}$)	197 (100, 21)	221 (102, 21)	222 (101, 21)	228 (108, 23)	0.74

*PSV_5 = pressure support ventilation at 5 cm H_2O, $CPAP_{CF-5}$ = continuous positive airway pressure on continuous flow with 5 cm H_2O; $CPAP_{DV-5}$ = CPAP on Siemens Servo 900C with 5 cm H_2O.
†Values are means (SD, SEE).

Table 3. Sample with Standard Deviation and Standard Error of Estimate for Tidal Volume (V_T), Respiratory Rate (RR), Minute Ventilation ($\dot{V}_E$), Auto-PEEP, Effective Dynamic Compliance (C_{dyn}), Duty Cycle (T_I/T_{TOT}), and Rapid Shallow Breathing Index (RSB) among Various Modes in 23 Patients

	PSV_5*	$CPAP_{DV-5}$	$CPAP_{CF-5}$	T-Piece	p Value
V_T (mL)	461 (131, 27)	450 (162, 34)	391 (141, 29)	400 (128, 27)	0.25
RR (breaths/min)	23 (7, 1.5)	23 (7, 1.4)	24 (8, 1.6)	24 (7, 1.5)	0.98
$\dot{V}_E$ (L/min)	9.8 (2.2, 0.5)	9.7 (2.3, 0.5)	8.3 (2.0, 0.4)	8.6 (2.3, 0.5)	0.05
Auto-PEEP (cm H_2O)	4.6 (3.4, 0.7)	4.8 (2.7, 0.6)	3.1 (2.4, 0.5)	3.4 (3.1, 0.7)	0.15
C_{dyn} (mL/cm H_2O)	71 (38, 8)	80 (41, 8)	79 (48, 10)	81 (53, 11)	0.89
T_I/T_{TOT}	35 (4, 1)	37 (5, 1)	38 (5, 1)	38 (7, 1)	0.22
RSB (breaths/min/L)	58 (30, 6)	58 (30, 6)	72 (44, 9)	71 (45, 9)	0.39

*PSV_5 = pressure support ventilation at 5 cm H_2O, $CPAP_{CF-5}$ = continuous positive airway pressure on continuous flow with 5 cm H_2O, $CPAP_{DV-5}$ = CPAP on Siemens Servo 900C with 5 cm H_2O.
†Values are means (SD, SEE).

fully weaned with a Puritan Bennett 7200a, 7 of whom had chronic obstructive pulmonary disease.[18] They reported a reduction in PTP with flow-triggered CPAP when compared to a T-piece. They attributed this reduction to improvement in pulmonary mechanics. The reduction with PSV when compared to T-piece was attributed to the mechanical ventilator's assuming part of the work. In our heterogeneous group of patients, pulmonary mechanics in all the modes and T-piece were not different, which may explain the finding of no differences among the various modes and T-piece. Other differences between our study and the study of Sassoon et al are the type of ventilator and CPAP system used.

Total WOB in patients breathing spontaneously on mechanical ventilation includes physiologic WOB and imposed WOB.[23] Physiologic WOB is primarily determined by respiratory resistance, respiratory compliance, and the presence of auto-PEEP. Normal physiologic WOB in healthy individuals is reported to be 0.3-0.6 J/L.[24] Fiastro and associates found that patients are weaned successfully when the WOB value is lower than 1.44 J/L or 16 J/min.[19] Imposed WOB can be ≥ the physiologic WOB.[25] The major determinates of imposed WOB are the flow-resistive properties of the ventilatory circuit, breathing circuit, and/or tracheal tube. In patients breathing with a T-piece, the imposed WOB is primarily due to the tracheal tube and breathing circuit.[26] In patients breathing with continuous-flow CPAP, in addition to the tracheal tube and breathing circuit, the imposed WOB depends on the fluctuation of airway pressure during the breathing cycle due to inadequate patient peak inspiratory flow[27] and an external PEEP-valve.[28] While breathing with the Siemens Servo 900C, the imposed WOB depends upon the tracheal tube, the pressure drop from baseline, and the time elapsed from the onset of patient effort until the ventilator delivers a flow of gas.[29]

The imposed WOB is not constant, and it can increase or decrease depending upon patient peak flow demand. Although we did not divide the total WOB into the individual components, the physiologic WOB and the imposed WOB—we attributed the small increase in total WOB above the normal range in all the modes and T-piece to auto-PEEP and/or imposed WOB. We believe that through the gradual unloading of the ventilatory muscles, which improved respiratory muscle performance, the patients' ventilatory demands were met adequately to overcome modest imposed WOB when they were placed on low-levels PSV, CPAP, and T-piece. This may be one of the reasons why all patients were comfortable on various modes and T-piece. However if ventilatory demands had not been met adequately, patients might have become markedly tachypneic with modest amount of imposed WOB.[30] The lack of increase in respiratory rate or other measures of pulmonary mechanics among various modes and T-piece suggests that the set inspiratory flow was adequate to meet the patients' peak inspiratory flow. The presence of a small amount of auto-PEEP in our patients on various modes and T-piece could be due to expiratory flow resistance from the ventilatory circuit, the breathing circuit, or the tracheal tube, and/or from the respiratory airway resistance. Auto-PEEP in our patients was not statistically different among various modes and T-piece. It is possible that the presence of a small amount of auto-PEEP on various modes and T-piece could affect the individual total WOB.

There may be several other reasons why we found no differences in our group of patients among the various modes and T-piece. Similarities in results between PSV_5 and T-piece might be from the beneficial effect of PSV with the Siemens Servo 900C on the WOB, which may have been offset by the amount of work done to trigger the ventilator for the delivery of gas flow. Also, the presence of auto-PEEP might have improved WOB by improving the functional residual capacity while on T-piece. The absence of difference between PSV_5 and $CPAP_{DV-5}$ might have been due to a low level of airway pressure maintained by the Siemens Servo 900C throughout inspiration, once the ventilator was triggered.[16,31] The presence of auto-PEEP during PSV and CPAP on Siemens Servo 900C might have interfered with the trigger mechanism, thereby increasing WOB. However, this increase in WOB from auto-PEEP might have been reduced with PSV by over-

coming some of the flow-resistive work, whereas the WOB from auto-PEEP on CPAP might have been reduced because the set PEEP might have helped to overcome most of the auto-PEEP. Thus, the net result on total WOB from PSV and CPAP might have been equivalent.

The optimum level of CPAP in improving gas exchange and pulmonary mechanics varies in patients recovering from acute respiratory failure.[6] Although we did not measure arterial blood gases, arterial oxygen saturation in all modes and T-piece remained the same. Our study, like others,[9-11] shows that $CPAP_{DV-5}$ is comparable to $CPAP_{CF-5}$. The validity of the comparison depends on the efficacy of the CPAP system used. Our system consists of a DFG with a non-reservoir circuit and an external PEEP valve with a spring loaded threshold resistor. DFG delivers 75-100 L/min of flow that can be adjusted manually to meet to the patient's peak flow demand.[32] Hillman and co-workers[33] demonstrated that a CPAP system with 75 L/min of continuous flow with a non-reservoir circuit and a threshold PEEP valve of 5 cm of H_2O is efficient in maintaining constant airway pressure.

Our study differs from that of Viale et al,[12] who reported that the imposed WOB in patients being weaned from the Siemens Servo 900C on $CPAP_{DV-5}$ (0.27 + 0.04 J/L) was different from that on the $CPAP_{CF-5}$ (0.19 + 0.02 J/L). They did not measure the total WOB and, therefore, increases in imposed WOB, which they reported to be statistically significant, may be clinically unimportant as a proportion of the total WOB. Working pressures and types of humidifier were not reported in their study but could affect the imposed WOB.

Conclusion

Although the mechanisms of maintaining positive airway pressure is different with PSV_5, $CPAP_{CF-5}$, and $CPAP_{DV-5}$, our study shows that, the WOB and the PTPs are comparable with that of the T-piece, a spontaneous breathing mode. This is to be expected. When the patient's ventilatory demands are met adequately to overcome modest imposed WOB, then various modes and T-piece should play an unimportant role in potentially fatiguing the patient. From our study, we can postulate that following gradual weaning with PSV when adequate ventilatory demands are met and when respiratory muscle performance is good, trials with T-piece or 5 cm H_2O of CPAP (instead of 5 cm H_2O of PSV on the Siemens Servo 900C) may offer no benefit prior to extubation or decannulation. This remains to be proven. It is important to note that, although our study showed no statistical difference among various mode and T-piece, clinically important differences could exist among various modes and T-piece when the peak inspiratory flow and other ventilatory demands are not met adequately or respiratory muscle performance is poor. To our knowledge, this is the only clinical study that demonstrates that at 5 cm H_2O, WOB and PTP on the Siemens Servo 900C CPAP mode are comparable to those of a continuous-flow CPAP system, using adjustable DFG with a non-reservoir circuit and an external PEEP valve.

PRODUCT SOURCES

Ventilator:
Servo 900C, Siemens-Elema AB, Sweden

CPAP System:
Adjustable Downs flow generator, #9250, Vital Signs Inc, Totowa NJ
External PEEP valve, #9005, Vital Signs Inc, Totowa NJ

Pulmonary Mechanics Monitor:
Model CP-100, Bicore Monitoring Systems, Irvine CA

Esophageal Balloon Catheter:
Smart Cath, Bicore Monitoring Systems, Irvine CA

Pneumotachograph:
VarFlex, Bicore Monitoring System, Irvine CA

Humidifier:
RCI Conchatherm III, Respiratory Care Inc, Arlington Height IL

REFERENCES

1. Slustky AS. Mechanical ventilation. American College of Chest Physicians' Consensus Conference. Chest 1993;104(6):1833-1859. *See the published erratum in Chest 1994;106(2):656.*
2. Marini JJ. Weaning techniques and protocols. Respir Care 1995; 40(3):233-238.
3. Petros AJ, Lamond CT, Bennett D. The Bicore pulmonary monitor. A device to assess the work of breathing while weaning from mechanical ventilation. Anaesthesia 1993;48(11):985-988.
4. Nathan SD, Ishaaya AM, Koerner SK, Belman MJ. Prediction of minimal pressure support during weaning from mechanical ventilation. Chest 1993;103(4):1215-1219.
5. Brochard L, Rua F, Lorino H, Lemaire F, Harf A. Inspiratory pressure support compensates for the additional work of breathing caused by the endotracheal tube. Anesthesiology 1991;75(5):739-745.
6. Katz JA, Marks JD. Inspiratory work with and without continuous positive airway pressure in patients with acute respiratory failure. Anesthesiology 1985;63(6):598-607.
7. Petrof BJ, Legare M, Goldberg P, Milic-Emili J, Gottfried SB. Continuous positive airway pressure reduces work of breathing and dyspnea during weaning from mechanical ventilation in severe chronic obstructive pulmonary disease. Am Rev Respir Dis 1990;141:281-289.
8. Quan SF, Falltrick RT, Schlobohm RM. Extubation from ambient or expiratory positive airway pressure in adults. Anesthesiology 1981;55(1):53-56.
9. Katz JA, Kraemer RW, Gjerde GE. Inspiratory work and airway pressure with continuous positive airway pressure delivery systems. Chest 1985;88(4):519-526.
10. Capps JS, Ritz R, Pierson DJ. An evaluation, in four ventilators, of characteristics that affect work of breathing. Respir Care 1987;32(11): 1017-1024.
11. Hillman DR, Breakey JN, Lam YM, Noffsinger WJ, Finucane KE. Minimizing work of breathing with continuous positive airway pressure and intermittent mandatory ventilation: an improved continuous low-flow system. Crit Care Med 1987;15(7):665-670.
12. Viale JP, Annat G, Bertrand O, Godard J, Motin J. Additional inspi-

ratory work in intubated patients breathing with continuous positive airway pressure systems. Anesthesiology 1985;63(5):536-539.
13. Viale JP, Annat GJ, Bouffard YM, Delafosse BX, Bertrand OM, Motin JP. Oxygen cost of breathing in postoperative patients. Pressure support ventilation vs continuous positive airway pressure. Chest 1988;93 (3):506-509.
14. Annat GJ, Viale JP, Dereymez CP, Bouffard YM, Delafosse BX, Motin JP. Oxygen cost of breathing and diaphragmatic pressure-time index. Measurements in patients with COPD during weaning with pressure support ventilation. Chest 1990;98(2):411-414.
15. Brochard L, Pluskwa F, Lemaire F. Improved efficacy of spontaneous breathing with inspiratory pressure support. Am Rev Respir Dis 1987; 136(2):411-415.
16. Hirsch C, Kacmarek RM, Stanek K. Work of breathing during CPAP and PSV imposed by the new generation mechanical ventilators: A lung model study. Respir Care 1991;36(8):815-828.
17. Lee KH, Hui KP, Lim TK, Tan WC. Work of Breathing during continuous positive airway pressure, pressure support ventilation, and T-piece during weaning from mechanical ventilation (abstract). Am Rev Respir Dis 1994;149:A67.
18. Sassoon CS, Light RW, Lodia R, Sieck GC, Mahutte CK. Pressure-time product during continuous positive airway pressure, pressure support ventilation, and T-piece during weaning from mechanical ventilation. Am Rev Respir Dis 1991;143(3):469-475.
19. Fiastro JF, Habib MP, Shon BY, Campbell SC, Comparison of standard weaning parameters and the mechanical work of breathing in mechanically ventilated patients. Chest 1988;94(2):232-238.
20. Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. A simple method for assessing the validity of the esophageal balloon technique. Am Rev Respir Dis 1982;126(5):788-791.
21. Petrini MF, Evans JN, Wall MA, Norman JR. A Gaussian method to improve work of breathing calculations. Biomed Instrum Technol 1995;29(1):55-62.
22. Collett PW, Perry C, Engel LA. Pressure-time product, flow, and oxygen cost of resistive breathing in humans. J Appl Physiol 1985;58(4): 1263-1272.
23. Banner MJ, Jaeger MJ, Kirby RR. Components of the work of breathing and implications for monitoring ventilator-dependent patients. Crit Care Med 1994;22(3):515-523.
24. Ballantine TV, Proctor HJ, Broussard ND, Litt BD. The work of breathing: potential for clinical application and the results of studies performed on 100 normal males. Ann Surg 1970;171(4):590-594.
25. Banner MJ, Kirby RR, Blanch PB, Layon JA. Decreasing imposed work of the breathing apparatus to zero using pressure-support ventilation. Crit Care Med 1993;21(9):1333-1338.
26. Bolder PM, Healy TE, Bolder AR, Beatty PC, Kay B. The extra work of breathing through adult endotracheal tubes. Anesth Analg 1986;65 (8):853-859.
27. Gherini S, Peters RM, Virgilio RW. Mechanical work on the lungs and work of breathing with positive end-expiratory pressure and continuous positive airway pressure, Chest 1979;76(3):251-256.
28. Banner MJ. Expiratory positive-pressure valves: flow resistance and work of breathing. Respir Care 1987;32(6):431-444.
29. Sassoon CSH, Mahutte CK. What you need to know about the ventilator in weaning. Respir Care 1995;40(3):249-256.
30. Kirton OC, DeHaven CB, Morgan JP, Windson J, Civetta JM. Elevated imposed work of breathing masquerading as ventilator weaning intolerance. Chest 1995;108(4):1021-1025.
31. Samodelov LF, Falke KJ. Total inspiratory work with modern demand valve devices compared to continuous flow CPAP. Intensive Care Med 1988;14(6):632-639.
32. Ward JJ, Awan ZI. Flow capabilities of the adjustable Downs flow generator(abstract). Respir Care 1987;32(10):906.
33. Hillman DR, Finucane KE. Continuous positive airway pressure: a breathing system to minimize respiratory work. Crit Care Med 1985;13(1):38-43.

RESPIRATORY CARE

Special Issue

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Safety of Intranasal Beclomethasone Dipropionate: A Review

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I. Introduction
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Introduction

Allergic rhinitis is a common chronic condition that affects more than 25 million persons in the United States[1] and is characterized by nasal obstruction and itching, sneezing, and rhinorrhea. Not only are these symptoms bothersome to patients, but they also may have a considerable social, medical, and economic impact on their lives.

In the United States, customary first-line therapy for the treatment of allergic rhinitis has been the use of antihistamines and/or decongestants. Drowsiness from the use of antihistamines and rebound congestion from the use of decongestants makes use of these therapies less than ideal. The nonsedating antihistamines such as terfenadine, which are available only through prescription, are being used increasingly. However, concerns about cardiac dysrhythmias with these agents have raised questions about their widespread use.[2]

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Although intranasal corticosteroids generally are recognized as being more effective than other topical medications, concern over their potential systemic side effects has limited their use. The first generation of topical steroids, such as prednisolone, dexamethasone, and betamethasone, was found to cause adrenal insufficiency in some patients.[3] The introduction to the United States in 1981 of beclomethasone dipropionate (BDP) as a pressurized intranasal spray represented an important advance in rhinitis therapy. In 1987, a suspension of BDP in an aqueous base for intranasal administration became available. This formulation is administered by a manually actuated pump and avoids the use of the propellant necessary in the pressurized spray, which may be an irritant to the nostrils of some patients.

Both the aerosol formulation of BDP (BDP-AE) and the aqueous formulation (BDP-AQ) have been used extensively for the treatment of allergic rhinitis and have been the topic of numerous clinical studies. This paper, which reviews the safety of intranasal BDP, evaluates the risks of adverse events that may occur following the systemic absorption of corticosteroids and the incidence of adverse events associated with the use of intranasal BDP.

The MEDLINE and Health databases of the worldwide medical literature published since 1966 were searched for articles on the intranasal administration of beclomethasone dipropionate as an aqueous spray or beclomethasone dipropionate monohydrate as an aerosol, for the treatment of allergic rhinitis. The

search terms included beclomethasone as the major topic with the additional restriction that the articles cover human clinical studies.

Adverse Events Resulting from the Systemic Absorption of BDP

A 1995 review[4] of the use of inhaled glucocorticoids for the treatment of asthma concluded that only with the use of "high" doses of inhaled glucocorticoids is there a risk of some of the adverse events associated with the use of orally administered glucocorticoids. Because only a small fraction of the intranasal dose of BDP probably is absorbed systemically, the expectation is that intranasal use of BDP at the recommended dose of 168-336 μg/day in the United States or 200-400 μg/day in Europe has a negligible risk of causing adverse events associated with the oral administration of glucocorticoids. Even though intranasal BDP has been available for more than 15 years, no studies were found that related the relative amounts of BDP absorbed following the administration of orally inhaled and intranasal doses of BDP.

Adrenal Suppression

Reports in the medical literature suggest that orally inhaled BDP and other steroids may have effects on adrenal function.[5] The extent to which glucocorticoid drugs suppress function of the hypothalamic-pituitary-adrenal (HPA) axis depends on the dose, duration, frequency, and timing of their administration.

In a review of the literature on the use of orally inhaled BDP for the treatment of asthma, Lipworth[6] concluded that in adults doses of up to 400 μg/day have no effect on HPA-axis activity and that HPA-axis suppression is extremely unlikely with inhaled doses of BDP below 800 μg/day in either adults or children. Reed[7] stated that, based on the review of a large number of studies, even small doses of 400 μg/day of orally inhaled BDP may suppress plasma or urinary cortisol to a statistically significant degree, but the clinical importance of this suppression is uncertain. However, cases of adrenal suppression in children using orally inhaled BDP have been reported with dosages of 400-2,000 μg/day,[8-10] and use of intranasal BDP at the recommended doses for allergic rhinitis (up to 400 μg/day) has not been associated with suppression of the HPA axis.[11-13]

Sorkin et al[14] noted that except in inordinately high doses, intranasal BDP should not cause adrenal suppression and that it has never been shown to cause clinical signs of adrenal suppression. The only exception to this was the case reported by these investigators who described a 27-year-old man with persistent fatigue and a history of long-standing nasal obstruction, frontal headaches, and postnasal discharge. The patient had multiple episodes of acute purulent sinusitis that required antibiotic therapy. He was placed on 400 μg/day intranasal BDP and after a few weeks was switched to flunisolide 0.025%, two sprays in each nostril twice daily. After 4 months he was switched back to BDP and 2 months later a test for serum cortisol level following adrenocorticotropic hormone (ACTH) administration showed a minimal rise in the level. Further testing confirmed the diagnosis of adrenal suppression.

In a study of 4 healthy subjects, Harris et al[15] showed that 9:00 AM plasma cortisol levels were reduced following intranasal BDP administration only at daily doses of at least 8 mg. In a second group of 5 healthy subjects, some reduction in 9:00 AM plasma cortisol levels was observed following oral inhalation of 1 mg BDP/day combined with the intranasal administration of 2 mg BDP/day.

Studies that compared the effects on plasma cortisol levels of intranasal BDP and intranasal placebo all have failed to find statistically significant effects.[16-22] These studies included patients treated with 336 μg/day BDP-AE for 6 months[22] and up to 800 μg/day BDP-AE for 2 weeks.[16]

Brannan et al[23] evaluated the effects of 336 μg BDP-AQ once daily, 168 μg BDP-AQ twice daily, placebo, and 10 mg/day oral prednisone on the plasma cortisol response to cosyntropin stimulation following treatment for 36 days. Cosyntropin stimulation is a sensitive and reproducible method used to determine the capacity of the adrenal glands to respond to stimulation and to assess the functional reserve of the adrenal cortex. There were no significant differences ($p > 0.05$) between each BDP-AQ group and the placebo group in their plasma cortisol response to cosyntropin stimulation. The response in the placebo group was significantly different ($p < 0.01$) from that in the prednisone group.[23]

Candida Infections

Localized *Candida* infections in the mouth, pharynx, and larynx have been associated with the use of BDP by oral inhalation. In 7 of the clinical studies reviewed[17,19,24-28] in which patients had nasal and/or pharyngeal cultures for *Candida*, no evidence was found for a definitive relationship between the use of intranasal BDP and *Candida* infection. None of the patients who had positive *Candida* cultures were identified as having clinical manifestations of a *Candida* infection. These 7 studies included 762 patients treated with 68-400 μg/day BDP, and 413 of them were treated with 300-400 μg/day BDP for at least 12 weeks.

Cataract Formation

The development of posterior subcapsular cataracts (PSC) is a recognized complication of the use of systemic corticosteroids.[29] The association between orally inhaled corticosteroid use and the development of PSCs comes from case reports.[30] Fraunfelder and Meyer[31] reported on 21 patients with bilateral PSCs who had used orally inhaled or intranasal BDP. These authors noted that most patients had used BDP for more than 5 years, often at higher than the recommended dosages, and that 9 of these patients also had received systemic cor-

ticosteroids. No other reports of PSCs following intranasal use of BDP were found in the medical literature.

Glaucoma

Although there is an established ocular hypertensive response to corticosteroids administered by various routes, a relationship to the use of intranasal BDP has not been established. Opatowsky et al[32] reported on two patients using intranasal BDP (dose not specified) who had increased intraocular pressure that returned to normal following discontinuation of BDP. No other reports of glaucoma in association with the use of intranasal BDP were found.

Behavioral Changes

The use of systemic corticosteroids has been associated with acute psychologic changes.[33] Other than two reports of mania reported in association with the use of BDP nasal spray,[34,35] no reports on other psychologic changes were found.

Osteoporosis

It is well known that the use of oral corticosteroids results in decreased bone density and puts patients at an increased risk of fractures of the vertebral spine, hip, and ribs. Glucocorticoids reduce bone mass directly by inhibiting bone formation and indirectly by inhibiting the secretion of androgen in the pituitary-gonadal and adrenal systems, by limiting calcium absorption in the intestines, and by limiting calcium reabsorption in the renal tubules.[36]

Studies that have investigated the effects of orally inhaled corticosteroids on biochemical markers of bone metabolism[37-39] have reported effects at dosages of at least 400 μg/day BDP. The relevance of these changes in terms of the risk of osteoporosis and fracture is uncertain, and the importance of the changes remains to be determined.

The only study found on the effects of intranasal BDP on markers of bone metabolism reported no significant effects in children with seasonal allergic rhinitis.[40] This study evaluated the effects on serum osteocalcin, parathyroid hormone, total alkaline phosphatase, bone alkaline phosphatase, and type-I collagen telopeptide of the use of 200 μg/day BDP-AE, 400 μg/day BDP-AE, and 30 mg/day sodium cromoglycate for 2 months in 39 children, 6-14 years of age. No statistically significant within-group changes occurred in any of the markers. There were occasional between-group differences that in the opinion of the investigators were "minor and probably clinically insignificant."

Growth

The prolonged use of systemic corticosteroids is known to affect linear growth. No studies reporting on growth among children receiving intranasal BDP were found in the medical literature.

Effects of Intranasal BDP on the Nasal Mucosa

Because the local application of corticosteroids may cause dermal atrophy, there has been a concern that the prolonged use of intranasal BDP might cause atrophic changes of the nasal mucosa. Most studies that have reported on the effects of BDP on the nasal mucosa were short-term. In studies of the long-term use of intranasal BDP for periods of 2 to 36 months,[21,22,24,41-43] no adverse effects on nasal mucosa (including mucosal atrophy) could be attributed to the use of intranasal BDP, based on biopsy findings.

Clinical Studies of BDP-AE and BDP-AQ

A computerized search of the medical literature identified 23 studies[17,19-23,44-60] in which BDP-AE (17 studies) and BDP-AQ (6 studies) were used for the treatment of allergic rhinitis. The search was limited to studies that included a placebo-treated group of patients to provide an assessment of the incidence of adverse events associated with the use of intranasal BDP. Adverse events that occurred in at least 1% of the patients treated with either BDP or placebo are summarized in Table 1 for studies of BDP-AQ, and in Table 2 for studies of BDP-AE.

Table 1. Adverse Event Occurring in at Least 1% of Patients in Comparative Studies of Intranasal Beclomethasone Aqueous Spray (BDP-AQ) and Placebo

Adverse Event	Number of Patients Affected (%) BDP-AQ (n = 393)*	Placebo (n = 371)
Epistaxis†	28 (7.1)	15 (4.0)
Nasal irritation, burning, stinging, soreness, dryness	14 (3.6)	20 (5.4)
Sore throat	10 (2.5)	5 (1.3)
Headache	32 (8.1)	18 (4.9)
Unpleasant smell	2 (0.5)	6 (1.6)
Total number of adverse events reported	95	89

* n = number of treated patients.
† Epistaxis includes bloody nasal discharge.

Many of the reported adverse events were minor. The data in Tables 1 and 2 suggest that many of the adverse events may have been due to the vehicle for BDP and/or the propellant used in the aerosol rather than to the active drug. No consistent pattern of differences was observed in the event rates for BDP-treated and placebo-treated patients. None of the reported adverse events were attributed to the systemic absorption of BDP (eg, skin thinning and easy bruising, various metabolic effects, and hematologic and immunologic effects) or to steroid

withdrawal. No cases of nasal septum perforation were reported, even though this event occasionally has been reported in association with the use of intranasal BDP.[61,62]

Table 2. Adverse Event Occurring in at Least 1% of Patients in Comparative Studies of Intranasal Beclomethasone Aerosol Spray (BDP-AE) and Placebo

Adverse Event	Number of Patients Affected (%) BDP-AE (n = 648)*	Placebo (n = 571)
Epistaxis†	10 (1.5)	11 (1.9)
Nasal irritation, stinging, dryness	28 (4.3)	35 (6.1)
Headache	9 (1.4)	8 (1.4)
Sneezing	35 (5.4)	46 (8.1)
Events not specified	29 (4.5)	38 (6.7)
Total number of adverse events reported	133	157

* n = number of treated patients.

† Epistaxis includes bloody nasal discharge.

The incidence of adverse events is in part related to the way in which the information was obtained. Most of the studies did not specify whether the information was obtained by direct or indirect questioning. The value of the data in Tables 1 and 2 is to provide information on the relative incidence of adverse events in BDP-treated and placebo-treated patients.

In studies of BDP-AE and placebo, epistaxis (nose bleed and/or blood-streaking of nasal discharge) was reported by 1.5% and 1.9% of the patients, respectively (Table 2). In a comparative study of BDP-AE and placebo[26] that was not included in Table 2 because it contained incomplete data on adverse events, information on epistaxis was obtained by use of a patient questionnaire. For patients who reported epistaxis before the start of the study, it became worse in 3 of 20 BDP-treated patients compared to 0 of 3 placebo-treated patients. Epistaxis was reported for 12 (43%) of 28 BDP-treated patients and for 4 (21%) of 19 placebo-treated patients who did not have epistaxis before the start of the study. Most of the episodes in all patients were slight, and often were only blood-streaking of nasal discharge.

As might be expected, most studies of intranasal BDP in which placebo groups were included were of short duration, usually 2-4 weeks. In 4 of the studies[17,22,24,25] summarized in Tables 1 and 2, patients were treated for at least 12 weeks. Although none of the studies provided data on adverse event rates for different durations of treatment, there was no indication that prolonged treatment was associated with an increase in the incidence of adverse events.

No studies of the safety of intranasal BDP in pregnant or geriatric (> 65 years of age) patients were identified. Many of the studies included older patients but did not separately evaluate adverse events for this group of patients. Four studies[45,50,57,60] were identified that evaluated the use of 168-400 μg/day BDP for 2-3 weeks in pediatric patients. None of these studies reported higher adverse event rates for the BDP-treated compared to the placebo-treated patients.

Commentary

Concerns have been expressed in the medical literature over the potential risks of topical corticosteroid use that may occur as a result of systemic absorption. Of note is the observation that none of the adverse events reported in the 23 studies of intranasal BDP that were reviewed was described as resulting from the systemic absorption of BDP. Review and critique of the published medical literature suggest that most adverse events associated with the use of either BDP-AQ or BDP-AE are minor, local and transient, and in the opinion of many investigators not of clinical importance. The studies reviewed did not in any way suggest that the prolonged use of intranasal BDP increases the risk of adverse events. No cases of clinical upper respiratory tract infection with *Candida*, clinically apparent adrenal suppression, or adverse events associated with "steroid withdrawal" following discontinuation of BDP were reported in any of the clinical studies of intranasal BDP reviewed.

No published studies were identified that addressed some aspect of the safety of intranasal BDP, such as its effects on linear growth and the risk of osteoporosis. It is probable that only a small amount of the intranasal dose is absorbed systemically, and the occurrence of these adverse events is rare even for patients administered orally inhaled BDP.[63] It would seem reasonable to conclude that the risk of any of these steroid-related adverse events must be rare among patients using intranasal BDP. The data reviewed for this paper cannot be used to predict any maximum safe dose of intranasal BDP in terms of preventing the occurrence of steroid-related adverse events. Data from studies of the inhaled use of BDP cannot be used because no studies (to our knowledge) have compared the relative amounts of systemic absorption of BDP when administered by inhalation and intranasally. One other aspect of the use of intranasal BDP that has not been assessed is the risk associated with the simultaneous use of inhaled and intranasal BDP. To avoid potential problems of overdosing with drugs such as BDP that are used for more than one indication, patients should be questioned about their use of all medications before new medications are prescribed.

The choice of whether to use the aqueous spray of BDP or the propelled dry powder is a matter of patient and physician preference. The aqueous spray probably is associated with less irritation to the nasal tissues, is easier to use, and causes less discomfort. The safety of intranasal BDP may further be enhanced by ascertaining that patients use the correct techniques for its administration and that they understand the adverse events that may occur following its use.

In summary, the use of intranasal BDP in doses of up to 400 μg/day for the treatment of allergic rhinitis appears to be a safe treatment and is without the risk of steroid-related

adverse events associated with the use of orally administered glucocorticoids.

REFERENCES

1. U.S. Bureau of the Census. Statistical abstract of the United States: 1990, 110th ed. Washington DC: Government Printing Office, 1990.
2. Monahan BP, Ferguson CL, Killeavy ES, Lloyd BK, Troy J, Cantilena LR Jr. Torsades de pointes occurring in association with terfenadine use. JAMA 1990;264(21):2788-2790.
3. Kobayashi RH, Kiechel F 3rd, Kobayashi AL, Mellion MB. Topical nasal sprays: treatment of allergic rhinitis. Am Fam Physician 50(1);1994:151-157, 161-162. *See the published erratum in Am Fam Physician 1994;50(8):1656-1658.*
4. Barnes PJ. Inhaled glucocorticoids for asthma. New Engl J Med 1995;332(13):868-875.
5. Mygind N. Local effect of intranasal beclomethasone dipropionate aerosol in hay fever. Br Med J 1973;4(890):464-466.
6. Lipworth BJ. Clinical pharmacology of corticosteroids in bronchial asthma. Pharmacol Ther 1993;58(2):173-209.
7. Reed CE. Glucocorticoids in asthma. Immunol Allergy Clin North Am 1993;13:903-915.
8. Law CM, Marchant JL, Honour JW, Preece MA, Warner JO. Nocturnal adrenal suppression in asthmatic children taking inhaled beclomethasone dipropionate. Lancet 1986;1(8487):942-944. *See the published erratum in Lancet 1987;1(8545):1321.*
9. Pfitis K, Everard ML, Milner AD. Unexpected side-effects of inhaled steroids: A case report. Eur J Pediatr 1991;150(6):448-449.
10. Phillip M, Aviram M, Lieberman E, Zadik Z, Giat Y, Levy J, Tal A. Integrated plasma cortisol concentrations in children with asthma receiving long-term inhaled corticosteroids. Pediatr Pulmonol 1992;12(2):84-89.
11. Francis RS. Adrenocortical function during high-dose beclomethasone aerosol therapy. Clin Allergy 1984;14(1):49-53.
12. Goldstein DE, Konig P. Effect of inhaled beclomethasone dipropionate on hypothalamic-pituitary-adrenal axis function in children with asthma. Pediatrics 1983;72(1):60-64
13. Pedersen S, Fuglsang G. Urine cortisol excretion in children treated with high doses of inhaled corticosteroids: a comparison of budesonide and beclomethasone. Eur Respir J 1988;1(5):433-435.
14. Sorkin S, Warren D. Probable adrenal suppression from intranasal beclomethasone. J Fam Pract 1986;22(5):449-450.
15. Harris DM, Martin I E, Harrison C, Jack D. The effect of intranasal beclomethasone dipropionate on adrenal function. Clin Allergy 1974;4(3):291-294.
16. Malm L, Wihl JA. Intra-nasal beclomethasone dipropionate in vasomotor rhinitis. Acta Allergol 1976;31(3):245-253.
17. Small P, Black M, Frenkiel S. Effects of treatment with beclomethasone dipropionate in subpopulations of perennial rhinitis patients. J Allergy Clin Immunol 1982;70(3):178-182.
18. Okuda M, Senba O. Effects of beclomethasone dipropionate nasal spray on subjective and objective findings in perennial allergic rhinitis. Clin Otolaryngol 1980;5(5):315-321.
19. Siegel SC, Katz RM, Rachelefsky GS, Geller BD, Montag I.L, Brandon ML, Cannon SJ. Multicentric study of beclomethasone dipropionate nasal aerosol in adults with seasonal allergic rhinitis. J Allergy Clin Immunol 1982;69(4):345-353.
20. Girard JP, Cuevas M, Heimlich EM. A placebo controlled double-blind trial of beclomethasone dipropionate in the treatment of allergic rhinitis. Allergol Immunopathol Madr 1978;6(2):109-114.
21. Gibson GJ, Maberly DJ, Lal S, Ali MM, Butler AG. Double-blind cross-over trial comparing intranasal beclomethasone dipropionate and placebo in perennial rhinitis. Br Med J 1974;4(5943):503-504.
22. van As A, Bronsky EA, Dockhorn RJ, Grossman J, Lumry W, Meltzer EO, Seltzer JM, Rogenes PR. Once daily fluticasone propionate is as effective for perennial allergic rhinitis as twice daily beclomethasone dipropionate. J Allergy Clin Immunol 1993;91(6):1146-1154.
23. Brannan MD, Herron JM, Reidenberg P, Affrime MB. Lack of hypothalamic-pituitary-adrenal axis suppression with once-daily or twice-daily beclomethasone dipropionate aqueous nasal spray administered to patients with allergic rhinitis. Clin Therapeu 1995;17:637-647.
24. Knight A, Kolin A. Long term efficacy and safety of beclomethasone dipropionate aerosol in perennial rhinitis. Ann Allergy 1983;50(2):81-84.
25. Lofkvist T, Svensson G. An open assessment of Becotide (beclomethasone dipropionate) nasal spray in seasonal allergic rhinitis. Acta Allergol 1975;30(4):227-238.
26. Brompton Hospital Medical Research Council Collaborative Trial. Double-blind trial comparing two dosage schedules of beclomethasone dipropionate aerosol with a placebo in the treatment of perennial rhinitis for twelve months. Clin Allergy 1980;10(3):239-251.
27. Brown HM, Storey G, Jackson FA. Beclomethasone dipropionate aerosol in treatment of perennial and seasonal rhinitis: a review of five years' experience. Br J Clin Pharmacol 1977;4(3, Suppl):283S-286S.
28. Bunnag C, Vipulakorn P, Pacharee P, Siriyananda C. Intranasal inhalation of beclomethasone dipropionate in the treatment of perennial rhinitis in adults. Ann Allergy 1980;44(2):100-105.
29. Hanania NA, Chapman KR, Kesten S. Adverse effects of inhaled corticosteroids. Am J Med 1995;98(2):196-208.
30. Russell G. Inhaled corticosteroid therapy in children: an assessment of the potential for side effects (editorial). Thorax 1994;49(12):1185-1188.
31. Fraunfelder FT, Meyer SM. Posterior subcapsular cataracts associated with nasal or inhalation corticosteroids. Am J Ophthalmol 1990;109(4):489-490.
32. Opatowsky I, Feldman RM, Gross R, Feldman ST. Intraocular pressure elevation associated with inhalation and nasal corticosteroids. Opthalmology 1995;102(2):177-179.
33. Mitchell DM, Collins JV. Do corticosteroids really alter mood? Postgrad Med J 1984;60(705):467-470.
34. Phelan MC. Beclomethasone mania (letter). Br J Psychiatry 1989;155:871-872.
35. Goldstein ET, Preskorn SH. Mania triggered by a steroid nasal spray in a patient with stable bipolar disorder (letter). Am J Psychiatry 1989;146(8):1076-1077.
36. Ip M, Lam K, Yam L, Kung A, Ng M. Decreased bone mineral density in premenopausal asthma patients receiving long-term inhaled steroids. Chest 1994.105(6):1722-1727.
37. Pavord I, Knox A. Pharmacokinetic optimization of inhaled steroid therapy in asthma. Clin Pharmacokinet 1993;25(2):126-135.
38. Geddes DM. Inhaled corticosteroids: benefits and risks (editorial). Thorax 1992;47(6):404-407.
39. McGill KA, Joseph B, Busse WW. Corticosteroids in the treatment of asthma. Practical recommendations. Clin Immunother 1995;4:16-48.
40. Martinati LC, Sette L, Chiocca E, Zaninotto M, Plebani M, Boner AL. Effect of beclomethasone dipropionate nasal aerosol on serum markers of bone metabolism in children with seasonal allergic rhinitis. Clin Exp Allergy 1993;23:986-991.
41. Bende M, Mark J. Long-term effects of topical corticosteroids in the nose. J Laryngol Otol 1992;106(9):810-812.
42. Mygind N, Sorensen H, Pedersen CB. The nasal mucosa during long-term treatment with beclomethasone dipropionate aerosol. A light- and scanning electron microscopic study of nasal polyps. Acta Otolaryngol Stockh 1978;85(5-6):437-443.
43. Poynter D. Beclomethasone dipropionate aerosol and nasal mucosa. Br J Clin Pharmacol 1977;4(3, Suppl):295S-301S.
44. Welsh PW, Stricker WE, Chu CP, Naessens JM, Reese ME, Reed

CE, Marcoux JP. Efficacy of beclomethasone nasal solution, flunisolide, and cromolyn in relieving symptoms of ragweed allergy. Mayo Clin Proc 1987;62:125-134.
45. Kobayashi RH, Tinkelman DG, Reese ME, Sykes RS, Pakes GE. Beclomethasone dipropionate aqueous nasal spray for seasonal allergic rhinitis in children. Ann Allergy 1989;62(3):205-208.
46. LaForce CF, Dockhorn RJ, Findlay SR, Meltzer EO, Nathan RA, Stricker W, et al. Fluticasone propionate: An effective alternative treatment for seasonal allergic rhinitis in adults and adolescents. J Fam Pract 1994;38(2):145-152.
47. Ratner PH, Paull BR, Findlay SR, Hampel F Jr, Martin B, Kral KM, Rogenes PR. Fluticasone propionate given once daily is as effective for seasonal allergic rhinitis as beclomethasone dipropionate given twice daily. J Allergy Clin Immunol 1992;90(3, Part 1):285-291.
48. Holopainen E, Malmberg H, Tarkiainen E. Experience of treating allergic rhinitis with intranasal beclomethasone dipropionate: Short-term trials and long-term follow-up. Acta Allergol 1977;32(4):263-277.
49. Blair H, Butler AG. Intranasal beclomethasone dipropionate in seasonal rhinitis in general practice. Practitioner 1976;216(1293):347-351.
50. Prahl P, Wilken-Jensen K, Mygind N. Beclomethasone dipropionate aerosol in treatment of hay fever in children. Arch Dis Child 1975; 50(11):875-878.
51. Cockcroft DW, MacCormack DW, Newhouse MT, Hargreave FE. Beclomethasone dipropionate aerosol in allergic rhinitis. Can Med Assoc J 1976;115(6):523-526.
52. D'Souza MF, Emanuel MB, Gregg J, Charlton J, Goldschmidt J. A method for evaluating therapy for hay fever. Clin Allergy 1983;13 (4):329-335.
53. Small P. Beclomethasone dipropionate nasal aerosol in adult patients with ragweed seasonal rhinitis. Ann Allergy 1982;49(1):20-22.
54. Small P, Barrett D. Effects of high doses of topical steroids on both ragweed and histamine-induced nasal provocation. Ann Allergy 1991;67(5):520-524.
55. Vilsvik JS, Jennssen AO, Walstad R. The effect of beclomethasone dipropionate aerosol on allergen induced nasal stenosis. Clin Allergy 1975;5(3):291-294.
56. Tarlo SM, Cockcroft DW, Dolovich J, Hargreave FE. Beclomethasone dipropionate aerosol in perennial rhinitis. J Allergy Clin Immunol 1977;59(3):232-236.
57. Smith JM, Clegg RT, Cook N, Butler AG. Intranasal beclomethasone dipropionate in allergic rhinitis. Br Med J 1975;2(5965):255.
58. Malm L, Wihl JA. Intra-nasal beclomethasone dipropionate in vasomotor rhinitis. Acta Allergol 1976;31(3):245-253.
59. Hansen I, Mygind N. Local effect of intranasal beclomethasone dipropionate aerosol in perennial rhinitis. Acta Allergol 1974;29(4):281-287.
60. Shore SC, Weinberg EG. Beclomethasone dipropionate aerosol in treatment of perennial allergic rhinitis in children. Arch Dis Child 1977;52(6):486-488.
61. Schoelzel EP, Menzel ML. Nasal sprays and perforation of the nasal septum (letter). JAMA 1985;253(14):2046.
62. LaForce C, Davis V. Nasal septal perforation in patients using intranasal beclomethasone dipropionate (BDP). J Allergy Clin Immunol 1985; 75:186.
63. Barnes PJ, Pedersen S. Efficacy and safety of inhaled corticosteroids in asthma. Report of a workshop held in Eze, France, October 1992. Am Rev Respir Dis 1993;148(4, Part 2):S1-S26.

RESPIRATORY CARE

Special Issue

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Respiratory Care Practitioners Can Provide Effective Smoking-Cessation Counseling to Hospitalized Smokers

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Hospitalization has been shown to be an ideal time to provide smoking-cessation counseling to patients. Many smokers stop on their own when hospitalized, and studies have shown that if smoking-cessation counseling is provided to interested patients during their hospitalization, a significant increase in the long-term cessation rate can be achieved. We base our Point of View on the results of a review of the literature on smoking cessation for hospital patients and a feasibility test in which counseling was provided by respiratory care practitioners (RCP) in 2 medium-sized hospitals. Elements of the intervention program included assessment of readiness to quit smoking (stage of change), a 20-minute bedside counseling session tailored to the patient's stage of change, a 10-minute videotape, a variety of written materials, and a follow-up phone call 1 to 3 weeks after the patient was discharged. Patient acceptance of the respiratory care counselors was high. Of the first 396 patients asked if they would be willing to meet with a smoking counselor, only 3% declined to be seen. Of those patients who were seen, 77% expressed a strong interest in quitting, 55% resolved to not smoke again, and 42% reported abstinence from tobacco at a follow-up interview 1 to 3 weeks after leaving the hospital. These encouraging short-term results demonstrate the feasibility of having RCPs deliver smoking-cessation counseling to hospitalized smokers. [Respir Care 1996; 41(11):1026-1029]

Background

As respiratory care practitioners know so well, cigarette smoking exacts a devastating toll on many smokers and from society as a whole. The negative effects extend beyond the individual smoker and include both the effects of 'passive' smoke on nonsmokers and the economic burden that smoking-related illness places on the health care system.[1] The economic benefits of smoking-cessation programs have been documented,[2] and the social benefits of preserved quality and length of life have been described as incalculable.[1]

Perhaps, one of the most powerful smoking-cessation strategies is to identify situations in which smokers are most likely to quit on their own and then to tailor an intervention to take advantage of what we might call teachable moments. Health care settings offer a variety of these opportunities. For example, brief advice to quit smoking delivered in the course of a routine outpatient visit significantly increases the proportion of smokers who quit permanently.[3] Quit rates can be improved if clinicians provide patients with assistance in quitting (eg, counseling and support) in addition to simple advice to quit.[4] The U.S. Preventive Services Task Force has recommended that to increase smoking-cessation rates, medical care patients should be exposed to a variety of intervention tech-

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niques on multiple occasions, delivered by both physicians and nonphysicians.[5] A meta-analysis by Kottke et al[4] found that increasing the number of contacts, the types of contacts, and the number of people making the contacts was the best way to increase the proportion of patients who quit smoking. They conclude that program development and program delivery is probably most fruitful when focused on presenting the nonsmoking message clearly, repeatedly, and consistently through multiple channels including personalized advice, printed materials, mass media; and on maintaining smoke-free medical, work, school, and home environments. A smoking-cessation clinical practice guideline, published in 1996 by the Agency for Health Care Policy and Research,[6] established recommendations that include using hospital personnel to implement these guidelines. The guidelines state "Specifically, clinicians and hospital administrators should collaborate to ensure that systems are in place that identify the smoking status of all patients admitted to a hospital and that provide at least a brief clinical intervention to every hospitalized patient who smokes."[6]

Hospitalization offers an excellent opportunity for smokers to quit permanently. Glasgow et al[7] found that even before hospital smoke-free policies were instituted, half of all smokers stopped during their hospital stay and 37% reported trying to quit or to remain off cigarettes following hospital discharge. A year after leaving the hospital, 16% were still not smoking. Patients who were older and were hospitalized with circulatory and respiratory diagnoses were consistently more likely to act to reduce cigarette smoking.[8] With the addition of a hospital smoking ban, the percentage of smokers temporarily stopping increased to about 80%, with those who continued to smoke typically reducing to only 1 or 2 cigarettes daily.[9]

Smoke-free environments, both in public places and within the hospital, have become a reality. Inclusion of requirements for smoke-free environments are now required for all hospitals seeking Joint Commission for Accreditation of Healthcare Organizations (JCAHO) accreditation.[6] However, a nonsmoking policy does not guarantee smoking-cessation interventions. Neighbor et al[8] found that less than 15% of hospitalized smokers in a smoke-free hospital received information about smoking cessation and means of abstaining during hospitalization, and none of the patients had smoking cessation included in their discharge planning.

For many smokers, hospitalization may prove to be one of the best "windows of opportunity for cessation interventions."[10] Orleans et al[11] noted that hospitalization is likely to raise perceived vulnerability to smoking-related diseases and responsiveness to medical advice to quit. Also, situations that promote abstinence, such as common diagnostic or therapeutic procedures (eg, oxygen therapy), are present during hospitalization.[12] Smoking-cessation intervention can be provided during hospitalization, when the patient is available and interested in quitting, rather than being scheduled for follow-up visits or clinic sessions that have been reported to have low compliance rates.[12] A descriptive study by Emmons and Goldstein[10] examined smoking prevalence and the role of hospital staff in promoting cessation. The results indicate that one third of smokers expressed interest in receiving cessation counseling from their physicians. Patient reports indicated that both physicians and nurses on the general medical unit intervened with smoking-cessation advice less frequently than did the staff of the cardiovascular disease unit.[10] Emmons and Goldstein further suggest that efforts to assist hospitalized smokers should focus on the development and evaluation of coordinated systems that provide self-help materials in addition to brief staff-delivered counseling. The value of brief bedside interventions has been established, but these interventions have generally been provided by special intervention teams—not general hospital staff. A study of a minimal-contact quit-smoking consult service provided results that compared favorably with those of more intensive treatments with similar patient groups.[12] Furthermore, these authors recognized that although the interventions were carried out by experienced counselors, the use of standardized protocols would facilitate the training of hospital nurses and allied health-care staff to carry them out.[12]

Orleans et al[11] noted that by 1993 only 6 controlled studies of inpatient interventions had been reported. One of these studies showed that a brief, bedside counseling session significantly increased 1-year quit rates among the general population of hospitalized smokers.[9] Intervention components included a 20-minute bedside counseling session and assessment of readiness to quit (ie, stage of change—precontemplator, contemplator, action, or maintenance), a 12-minute videotape, a variety of self-help materials, and a follow-up phone call a few weeks after hospital discharge. In addition to providing support for smoking cessation, the intervention addressed maintenance and avoidance of relapse. This intervention was delivered by health educators with extensive experience in smoking-cessation counseling. This randomized trial demonstrated the efficacy of a brief smoking-cessation intervention in a general hospital population and found that 1-year quit rates were increased by approximately 50% (9.2% quit in the usual care group, 13.5% quit in the counseling group).[9]

RCPs as Smoking-Cessation Counselors: A Feasibility Study

Many hospitals do not have experienced smoking-cessation counselors on their staff, and yet hospitalization offers an excellent opportunity to provide cessation counseling to patients. Given this problem, one attractive option would be to train selected members of the existing staff to provide counseling as a part of their duties. We sought to establish the feasibility of training RCPs for this new role.

In 1987, Nett[13] called this situation to the attention of RCPs by pointing out that while smoking cessation is the business of all health professionals, RCPs are in a unique position to

make a major difference in the American population. Smokers who are older and are hospitalized with circulatory and respiratory diagnoses are consistently more likely to act to reduce cigarette smoking.[8] These same patients constitute the service arena in which RCPs are most active and focused in delivery of patient care. We propose that RCPs, who often have the responsibility for treating these patients, are the most likely health professionals to provide smoking-cessation interventions to hospitalized smokers. In addition, the common pattern of RCP practice in providing specific therapies to many patients throughout the hospital is well suited to providing bedside smoking-cessation counseling to the general hospital population.[14,15]

Method

To investigate the practicality and effectiveness of having RCPs provide smoking-cessation counseling to the general population of hospital patients, a feasibility test is currently underway in the 2 Kaiser Permanente hospitals in Portland, Oregon. As a part of this research project, 6 RCPs have been trained to provide counseling using the model developed by Stevens et al.[9] Eligible patients include those who report being a smoker or recent quitter (within the past 3 months) at hospital admission, are 18 years of age or older, and have an expected hospital stay of at least 36 hours. Those excluded from this study include postpartum patients, the terminally ill, and those hospitalized for alcoholism, drug abuse, or mental illness.

Training of the selected RCPs was provided by health educators currently working in smoking-cessation programs in the Kaiser Permanente System. Training included attendance at a 9-session outpatient smoking-cessation program and a minimum of 10 hours of counseling hospital patients under the direction of an experienced counselor.

Elements of the hospital intervention included random assignment by identification number of all eligible patients to either an intervention or control group after hospital admission. As in the previous study in the same facilities,[9] the RCP interviewed and assessed the patient's readiness to quit smoking, engaged in a 20-minute bedside counseling session tailored to the patient's stage of change, provided the patient with a 12-minute videotape and a variety of written materials, and called the patient 2 to 3 weeks after the patient had left the hospital. Standardized rating systems were used by all of the RCPs in the study. Supervision of the RCPs and data collection is managed by the Kaiser Center for Health Research. Conditions of the study were approved by the Human Research Study Committee of Kaiser Permanente, Northwest Region.

Results

Patient acceptance of the respiratory care smoking counselor has been high with only 3% of the first 396 patients declining to see them. Of those patients seen, 77% expressed a strong interest in quitting smoking, 55% resolved not to smoke again, and 42% reported abstinence from tobacco at the follow-up telephone interview. These results compare favorably with the findings from the earlier study[9] in which health educators provided the counseling (Table 1). The RCP counselors were well accepted by the patients and the short-term results from this feasibility study are encouraging. Failure to see patients was definitely higher with the RCPs and warrants further investigation to identify barriers and improve access to patients.

Table 1. Comparison of Acceptance of the Inpatient Respiratory Care Practitioner to the Health Educator as Smoking-Cessation Counselor

	Smoking Counselor	Respiratory Care Practitioner
Number of participants in intervention program	435	525
Received counseling	80%	68%
Refused counseling	4%	3%
Not seen due to illness, logistical difficulties, short hospital stay	17%	29%

Discussion

Given the importance of smoking cessation and the increasing pressure to provide effective preventive medicine services, RCPs now have an opportunity to expand their scope of practice to include smoking-cessation counseling for hospitalized smokers. A longitudinal 4-year study at a large health maintenance organization demonstrated that successful cessation appears to halt the progressive increase in the use of both inpatient and outpatient health services associated with continued smoking.[2] In other words, managed care systems have learned that it is financially important to provide effective smoking-cessation programs for subscribers.

The type of counseling used in our study has been shown to be effective.[9] RCPs in this role are well accepted by patients, and the short-term results of their counseling results are promising. A coordinated hospital-wide smoking-cessation model could be integrated into existing staffing and scheduling for patient work by the respiratory care department. This would mean that systems already in place could offer this service rather than training an entire hospital staff or bringing in costly smoking-cessation specialists. Accountability for this type of patient intervention becomes clearly defined when the program is assumed by the respiratory care department and is not diffused by expecting all hospital staff to provide some type of intervention.

Although we have not yet collected cost data on the described intervention, costs include (1) patient counseling

time (about 30 min), (2) the videotape and player, (3) the self-help brochures and other materials, and (4) the cost of training RCPs (about 30 hours/RCP). Because RCPs are already on site in the hospital, we anticipate that using them can be cost effective. Also, RCPs have first-hand knowledge regarding the health effects of cigarette smoking because much of RCP practice is focused on smoking-related cardiac and pulmonary diseases. Further the continuous quality improvement program of the respiratory care department should allow monitoring of resources, interventions, and resultant outcomes for the entire hospital.

RCPs have an opportune moment to intervene with the parents of children hospitalized with a respiratory disease. The relationship of smoking by parents to the incidence of pediatric respiratory disease is well documented and again addresses the prevention aspect of disease control and health promotion.[16]

Objective measurements of pulmonary status including pulmonary function tests and carbon monoxide levels can by provided by RCPs—feedback that makes real the smoking health risks to the patient. Such feedback has proven a highly effective motivator for outpatients with respiratory disease.[17]

Conclusion

Smoking-cessation counseling represents an important and feasible expansion of the RCP's scope of practice. Further work is needed to identify the long-term outcomes of such interventions utilizing RCPs as smoking-cessation counselors and to resolve access/scheduling problems as identified in this research. RCPs in this study noted that their training and experience in this specific health prevention practice has proved helpful in dealing with other patient needs, eg, patient health education.

In this particular study, patient-focused care strategies including effective communication skills are emphasized. In addition, the RCP works in collaboration with the patient to determine future goals and skills necessary to achieve the goals of the patient. In other words, the RCP can move from the reactive mode of treating the consequences of disease to that of the proactive and knowledgeable health care professional actively engaged in the reduction and prevention of disease and the promotion of good health for the entire community.

We believe that smoking-cessation methodology and skills should be provided as part of the formal education of respiratory care practitioners. Such disease intervention and prevention can provide a new and promising facet of practice for the respiratory care profession.

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REFERENCES

1. Koop CE. Introduction: the effects of cigarette smoking—a global perspective. Am J Med 1992;93(Suppl 1):1S.
2. Wagner EH, Curry SJ, Grothaus L, Saunders KW, McBride CM. The impact of smoking and quitting on health care use. Arch Intern Med 1995;155(16):1789-1795.
3. Schwartz JL. Methods of smoking cessation. In: Fiore MC, editor. The medical clinics of North America: cigarette smoking—a clinical guide to assessment and treatment. Philadelphia: WB Saunders Company, 1992.
4. Kottke TE, Battista FN, DeFriese GH, Brekke ML. Attributes of successful smoking-cessation interventions in medical practice. A meta-analysis of 39 controlled trials. JAMA 1988;259(19):2883-2889.
5. US Department of Health and Human Services. The health consequences of involuntary smoking: a report of the surgeon general. Washington DC: USDHHS, Pub. No. (CDC)87-8398, 1986.
6. Fiore MC. Smoking-Cessation Clinical Practice Guideline Panel and Staff. The agency for health care policy and research smoking-cessation clinical practice guideline. JAMA 1996;275(16):1270-1280.
7. Neighbor WE Jr, Stoop DH, Ellsworth A. Smoking-cessation counseling among hospitalized smokers. Am J Prev Med 1994;10(3):140-144.
8. Glasgow RE, Stevens VJ, Vogt TM, Mullooly JP, Lichtenstein E. Changes in smoking associated with hospitalization: quit rates, predictive variables and intervention implications. Am J Health Promotion 1991;6(1):24-29.
9. Stevens VJ, Glasgow RE, Hollis JF, Lichtenstein E, Vogt TM. A smoking-cessation intervention for hospital patients. Med Care 1993;31(1):65-72.
10. Emmons KM, Goldstein MG. Smokers who are hospitalized: a window of opportunity for cessation interventions. Prev Med 1992;21(2):262-269.
11. Orleans CT, Rotberg HL, Quade D, Lees P. A hospital quit-smoking consult service: clinical report and intervention guidelines. Prev Med 1990;19(2):198-212.
12. Orleans CT, Kristeller JL, Gritz ER. Helping hospitalized smokers quit: new directions for treatment and research. J Consult Clin Psychol 1993;61(5):778-789.
13. LM. A new role for the respiratory therapist in smoking cessation (editorial). Respir 1987;32(11):1009-1010.
14. American Association for Respiratory Care. Clinical practice guideline: training health care professional for the role of patient and caregiver educator. Respir Care 1996;41(7):654-657.
15. American Association for Respiratory Care. Clinical practice guideline: providing patient and caregiver training. Respir Care 1996;41(7):658-662.
16. Cunningham J, O'Connor GT, Dockery DW, Speizer FE. Environmental tobacco smoke, wheezing and asthma in children in 24 communities. Am J Respir Crit Care Med 1996;153(1):218-214.
17. Risser NL, Belcher DW. Adding spirometry, carbon monoxide, and pulmonary symptom results to smoking-cessation counseling: a randomized trial. J Gen Int Med 1990;5(1):16-22.

Letters

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Pulse Oximeter Manufacturer Objects

The paper titled, "Evaluation of a Commercial Standard for Checking Pulse Oximeter Performance," published in the February issue of the Journal [Respir Care 1996;41 (2):100-104], has caused concern among some of our customers regarding the accuracy of Novametrix pulse oximeters by inferring that Novametrix pulse oximeters do not perform to our own specifications. Novametrix pulse oximeter sensors utilize light emitting diodes that operate at wavelengths of 660 and 940 nm, not at the 660 and 920 nm wavelengths that are utilized by Nonin pulse oximeters. The Nonin Finger Phantom simulates blood absorption at the Nonin red and infrared wavelengths; so it is hardly surprising that Novametrix sensors perform poorly when tested at these wavelengths. I would like to point out that Nonin provides a disclaimer on Page 5 of the Finger Phantom's Instruction and Service Manual:

> Minor S_{pO_2} variations will be seen between oximeter manufacturers because standards correlating red and infrared light absorption to oxygen saturation in pulse oximetry are not available. Each manufacturer has developed its own correlation and inevitably some differences have developed (see *Health Devices*, June 1989).

This difference should be kept in mind when commercial devices, such as the Nonin Finger Phantom, are marketed to work on all manufacturers' pulse oximeters. The best way to ensure pulse oximeter performance is to use the test equipment provided by pulse oximeter manufacturers for their particular unit.

Philip F Nuzzo
Director of Marketing
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Wallingford, Connecticut

Co-author Chatburn responds:

Perhaps our study is confusing because we are accustomed to seeing studies of new measuring devices compared with familiar standards. Such studies have become common with the recent interest in point-of-care testing.[1,2] In these studies, repeated measurements of the same standard value are employed to construct error intervals.[3] The error intervals quantitate bias and imprecision so that the instrument can be judged as either accurate or inaccurate. Our study was novel. It was designed to answer the opposite question: given a familiar measuring device, how adequate is a new standard made to spot check it? The confusing part is that we have to use the same repeated measurements and error intervals, but instead of interpreting the bias and imprecision as qualities of the measuring device, we view them in light of other error intervals (created by the instrument manufacturers with accepted gold standard techniques). The new standard is, thus, judged as either adequate or not.

Mr Nuzzo says that our paper has caused concern by inferring that Novametrix pulse oximeters do not perform to their own specifications. We trust that Mr Nuzzo means the customers infer this—not our paper. The casual reader of our paper might, for instance, look at our Figure 2 and see observed inaccuracy intervals compared to manufacturer's specifications. Not reading or, perhaps, not understanding the introduction or the discussion, one might miss some key points in interpreting our results. So, when Mr Nuzzo says that "...it is hardly surprising that Novametrix sensors perform poorly when tested at these wavelengths," he (perhaps like his customers) is assuming the study was about oximeter performance. The study did not evaluate performance of oximeters. The study evaluated the performance of the Finger Phantom (ie, its ability to reflect manufacturers' specifications and, thus, detect properly functioning oximeters). That is why the title was worded "Evaluation of a Commercial Standard..." And, that is why the conclusion is worded as it was. "Spot checks ... with the Finger Phantom are probably adequate for evaluating the performance of all devices in this study." In other words, the Finger Phantom performed adequately when used to detect well-functioning oximeters.

In the introduction, we said the purpose of the study was to determine whether the Finger Phantom could reproduce the error specifications supplied by the manufacturers. In the discussion, we explained that, "The specified saturation of each Finger Phantom was treated mathematically as the standard or true value for the purpose of creating inaccuracy intervals. However, the observed inaccuracy intervals were ultimately compared to the intervals derived from the pulse oximeter manufacturers' specifications, *assuming the latter to be 'true.'* (Emphasis added.) Furthermore, we were careful to point out that the "...major assumption of the study design..." was that the oximeters used were functioning correctly and that the manufacturers' specifications were valid.

We are grateful to Mr Nuzzo for pointing out the specific reasons why the Finger Phantom did not perform the same way with all oximeters (due to differences in LED output wavelengths) and for calling attention to the possibilities of misinterpreting some fairly abstract statistical concepts. It just shows that using even the simplest appearing technical device requires some theoretical understanding and careful thought on the part of health care professionals. As respiratory therapists, we need to make the effort to acquire and use this understanding if we are to continue to add real value to patient care.

If we yield to the seduction of simply using new technology without truly understanding it, we will become its slaves rather than its masters. And, because technology pervades every aspect of our lives, we risk losing the creative impulse that has brought us this far. How many college program directors are complaining that new students don't have the basic reading and math skills to get through introductory courses? How many of us have VCRs with clock displays perpetually flashing 12:00? I am reminded of one of my favorite science fiction short stories. Titled, "The Little Black Bag," it was written by CM Kornbluth in 1950.[4] The future course of technological civilization is predicted:

> After twenty generations of shilly-shallying and 'we'll cross that bridge when we come to it,' genus *homo* had bred itself into an impasse. Dogged biometricians had pointed out with irrefutable logic that mental sub-

normals were outbreeding mental normals and supernormals, and that the process was occurring on an exponential curve. Every fact that could be mustered in the argument proved that genus *homo* was going to wind up in a preposterous jam quite soon. If you think that had any effect on breeding practices, you do not know genus *homo*.

There was, of course, a sort of masking effect produced by that other exponential function, the accumulation of technological devices. A moron trained to punch an adding machine seems to be a more skillful computer than a medieval mathematician trained to count on his fingers. A moron trained to operate the twenty-first century equivalent of a linotype seems to be a better typographer than a Renaissance printer limited to a few fonts of movable type. This is also true of medical practice.

It was a complicated affair of many factors. The supernormals 'improved the product' at a greater speed than the subnormals degraded it, but in smaller quantity because elaborate training of their children was predicted on a custom-made basis. (*A premonition of home schooling?*) The fetish of higher education had some weird avatars by the twentieth generation: 'colleges' where not a member of the student body could read words of three syllables: 'universities' where such degrees as 'Bachelor of Typewriting,' 'Master of Shorthand' and 'Doctor of Philosophy (Card filing)' were conferred with the traditional pomp. The handful of supernormals used such devices in order that the vast majority might keep some semblance of social order going.

The "Little Black Bag" of the story was a doctor's bag containing miraculous instruments that worked independently, requiring little more than rudimentary reading skills and a pair of hands to support them. It had powerful medicines prescribed by simply matching the organ system to the symptom on a little card. Scalpels sank into flesh without leaving a mark, magically cutting only the diseased tissue and pushing aside blood vessels, muscular, and nervous tissue. Internal disorders were diagnosed automatically by simply placing a small imaging disk on the skin. The bag was accidentally transported back in time to our own era. Naturally, greed and ignorance destroyed the one who found it.

(As I was typing this I hit the letters "hte" and the computer automatically changed it to "the"! I was surprised because I hadn't read that part of the operator's manual that explained it.)

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REFERENCES

1. Connelly NR, Magee M, Kiessling B. The use of the iSTAT portable analyzer in patients undergoing cardiopulmonary bypass. J Clin Monitor 1996:12:311-315.
2. Wahr JA, Lau W, Tramper KK, Hallock L, Smith K. Accuracy and precision of a new portable handheld blood gas analyzer, the IRMA. J Clin Monitor 1996:12:317-324.
3. Chatburn RL. Evaluation of instrument error and method of agreement. JAANA 1996:64(3):261-268.
4. Silverberg R. Science fiction hall of fame. New York: Avon Books, 1793:410-439.

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RETROSPECTROSCOPE

Roast Pig and Scientific Discovery Part I

Mankind, says a Chinese manuscript ... for the first seventy thousand ages ate their meat raw, clawing or biting it from the living animal. ... The manuscript goes on to say that the art of roasting, or rather broiling (which I take to be the elder brother) was accidentally discovered in the manner following. The swine-herd, Ho-ti, having gone out into the woods one morning, as his manner was, to collect mast for his hogs, left his cottage in the care of his eldest son Bo-bo, a great lubberly boy, who being fond of playing with fire, as younkers of his age commonly are, let some sparks escape into a bundle of straw, which kindling quickly, spread the conflagration over every part of their poor mansion, till it was reduced to ashes. Together with the cottage ... what was of much more importance, a fine litter of new-farrowed pigs, no less than nine in number perished. ... Bo-bo was in utmost consternation, as you may think, not so much for the sake of the tenement, which his father and he could easily build up again with a few dry branches, and the labour of an hour or two, at any time, as for the loss of the pigs. While he was thinking what he should say to his father, and wringing his hands over the smoking remnants of one of those untimely sufferers, an odor assailed his nostrils, unlike any scent which he had before experienced. What could it proceed from?—not from the burnt cottage—he had smelt that smell before—indeed this was by no means the first accident of the kind which had occurred through the negligence of this unlucky young firebrand. Much less did it resemble that of any known herb, weed, or flower. A premonitory moistening at the same time overflowed his nether lip. He knew not what to think. He next stooped down to feel the pig, if there were any signs of life in it. He burnt his fingers, and to cool them he applied them in his booby fashion to his mouth. Some of the crumbs of the scorched skin had come away with his fingers, and for the first time in his life (in the world's life, indeed, for before him no man had known it) he tasted—*crackling!* Again he felt and fumbled at the pig. It did not burn him so much now, still he licked his fingers from a sort of habit. The truth at length broke into his slow understanding, that it was the pig that smelt so, and the pig that tasted so delicious; and surrendering himself up to the newborn pleasure, he fell to tearing up whole handfuls of the scorched skin with the flesh next it, and was cramming it down his throat in his beastly fashion, when his sire entered amid the smoking rafters, armed with retributory cudgel, and finding how affairs stood, began to rain blows upon the young rogue's shoulders, as thick as hailstones, which Bo-bo heeded not any more than if they had been flies. The tickling pleasure which he experienced in his lower regions had rendered him quite callous to any inconveniences he might feel in those remote quarters. His father might lay on, but he could not beat him from his pig, till he had fairly made an end of it, when, becoming a little more sensible of his situation, something like the following dialogue ensued.

"You graceless whelp, what have you got there devouring? Is it not enough that you have burnt me down three houses with your dog's tricks, and be hanged to you! but you must be eating fire, and I know not what—what have you got there, I say?"

"O, father, the pig, the pig! do come and taste how nice the burnt pig eats."

Bo-bo, whose scent was wonderfully sharpened since morning, soon raked out another pig, and fairly rending it asunder, thrust the lesser half by main force into the fists of Ho-ti, still shouting out "Eat, eat, eat the burnt pig, father, only taste—O Lord!"—with such-like barbarous ejaculations, cramming all the while as if he would choke. ...

In conclusion (for the manuscript here is a little tedious), both father and son fairly set down to the mess, and never left off till they had despatched all that remained of the litter. (1)

Part I is reprinted with permission of the American Lung Association from Am Rev Respir Dis 1977;115:853-860, and Part II from Am Rev Respir Dis 1977;115:1035-1044.

Charles Lamb, in his "Dissertation upon Roast Pig" then continues his narration: Ho-ti's cottage was from that time on quickly rebuilt and just as quickly burnt down, until soon father and son were haled into court along with the atrocious evidence (burnt pig). Within a few days after the trial (during which the jury acquitted both father and son) the judge's and jury's houses were a-burning and "there was nothing to be seen but fires in every direction. ... Eventually, a sage arose who made a discovery that the flesh of swine, or indeed of any other animal, might be cooked (burnt, as they called it) without consuming a whole house."

This is one of the earliest accounts of our theme in this and next month's *Retrospectroscope*—the role of *Chance* in scientific discovery and the wondrous benefits to mankind that accrue from it. Some like to call it "serendipity"—a word coined by Horace Walpole in 1754, based on the title of a fairy tale, "The Three Princes of Serendip," (the former name of Ceylon) the heroes of which were always making discoveries, by accidents and sagacity, of things they were not in quest of—the faculty of making happy and unexpected discoveries. The definition comes from the *Oxford English Dictionary*; some wag's more recent definition is that serendipity is looking for a needle in a haystack but coming up with the farmer's daughter. (I accept the latter only if modified to read—"but coming up with an ugly toad which the finder recognizes as the farmer's beautiful daughter and miraculously converts toad to daughter.")

So many have written on *Chance* or *Serendipity* in science that, in writing once more, I should do more than entertain you with the same or additional stories. Because the main purpose of my peering into a retrospectroscope is to examine the past to learn a lesson or two that will help us in the present and future, this look should lead to some useful, or at least controversial, recommendations. It will, but not until Part II, in next month's issue. First, I want to give examples of two types of discoveries in which chance played an important role: (A) some in which chance helped a scientist reach his committed goal or get to it more quickly and (B) those in which chance changed his goals and set him in a new direction.

A. Chance Speeded or Completed a Scientist's Ongoing Work

The Cholecystogram

Everyone who reads this journal knows that Evarts Graham was a leader of pulmonary surgery in this country. But he was more than that. In 1909, Abel and Rowntree had shown that chlorinated phenolphthaleins were excreted almost entirely in the bile and it occurred to Graham and his associates that if they could substitute a radiopaque element for chlorine, they should be able to get a roentgenographic shadow of the contents and contours of the gall bladder. The element they selected was iodine, and the compound sodium tetraiodophenolphthalein. Warren Cole, then a resident in surgery, did the injections.

> Six dogs were injected intravenously, and x-ray photographs were made of the gall bladder regions in all of them at frequent intervals after the injection. In five of the dogs no shadow was obtained, but fortunately a faint shadow was obtained in the sixth one. At first we were at a loss to understand why we had obtained a faint shadow in one dog but none at all in the other five animals. The idea then occurred to us that the reason for the failure was probably due to the fact that the animals were not fasting and that, therefore, the injected substance was not staying in the gall bladder for a long enough time to be concentrated and, therefore, to make a shadow. From the standpoint of the future development of cholecystography we often feel grateful to that one dog which cast a shadow, probably because he was accidentally given no food. If we had failed to get a shadow in all of these animals we probably should have abandoned the whole idea as a fruitless one. It is curious on how fragile a thread the destiny of some events hangs. When we came to investigate the matter we found that, as a matter of fact, through some mishap the animal keeper during the time of the experiment had for some reason neglected to feed the one dog on the morning of the injection but he had fed all of the others. Greater efficiency on the part of the animal keeper would doubtless have resulted in a complete failure of our experiment and, therefore, we would have given up the whole idea. Sometimes efficiency can be a curse. (2)

Staining of Tubercle Bacilli

On March 24, 1882, Robert Koch lectured to the Physiological Society of Berlin on the etiology of tuberculosis. After pointing out that one seventh of all people die of tuberculosis and that the mortality rate is especially high (one-third or more) for those in their potentially productive middle age years, he then described his method for staining tubercle bacilli in sputum and tissue (3). In the audience was Paul Ehrlich, whose 1878 doctoral thesis dealt with the affinity of dyes for specific tissues. After the lecture, Ehrlich went to his laboratory and set up slides covered with tuberculous sputum. He stained these according to Koch's directions and left them overnight on the cold laboratory stove. In the morning the charwoman in the laboratory started the fire, which speeded the staining by its effect on the waxy-coated bacteria so that when Ehrlich arrived, the tubercle bacilli were everywhere to be seen. On communicating this information and on showing the slides to Robert Koch, the latter became so impressed that he turned his investigations toward the causes underlying the disease rather than to mere descriptions of the effects of tuberculosis (4). Koch said, "We owe it to this circumstance alone that

it has become a general custom to search for the bacillus in sputum" (5).

Gram Stain

Beveridge (5) recounts the origin of this stain:

> A Danish physician, while staining bacteria, inadvertently took the wrong bottle from the rack and poured Lugol's iodine on a smear which he had been staining with gentian violet. Thinking his preparation had been spoilt, he tried to wash out the stain with alcohol so that he could start again. But when he examined the smear to see if he had decolourised it he found that many of the bacteria retained a deep purple colour. There is no need to tell readers who are bacteriologists that the name of the Dane was Gram, for the staining technique he developed as a result of this "accident" has made his name a familiar word in every bacteriological laboratory.

Positive Pressure Respiration

Alvan Barach devoted his medical lifetime to scientific and clinical pulmonary medicine and is especially known for his pioneering work on oxygen, helium-oxygen therapy, pressure breathing, and the equalizing-pressure chamber. He decided to be a pulmonary physician when he was five years old (that was in 1900) and watched his family physician terminate a severe attack of laryngeal dyspnea in his mother. His "one aim, one business, one desire" was to study breathing difficulties, as he put it years later (6).

Some years ago, he gave me this account of what he had learned from a patient. He was examining a patient with severe asthma (or emphysema) and noted that on every expiration, the patient pursed his lips and breathed out against this additional resistance. Barach thought this to be an unnecessarily tiring experience for his patient and said, "Look here. Watch how I breathe in and out—slowly and fully, with my mouth open—never through pursed lips. Now you do it." The good patient tried to emulate Barach's pattern and soon turned blue. Barach immediately realized the importance of the patient's pattern in maintaining a positive airway pressure during expiration and preventing early collapse of diseased airways. Barach "told it like it was" in 1938 (7), when he gave this as his explanation of why patients with asthma and emphysema so frequently pursed their lips during expiration and arbitrarily increased the resistance to the egress of air:

> This mechanism, developed by the patients themselves, appeared to have the physiological advantage of keeping open bronchiolar passageways, thereby producing a more efficient emptying of the alveolar air. It was suggested that the expiratory grunt in lobar pneumonia was a similar protective mechanism. Furthermore, it was found that patients with more or less continuous asthma of moderate degree will frequently obtain marked relief of their wheezing when they follow the instruction to breathe through partially closed lips for 3 to 10 minutes. The râles in expiration will at times clear up immediately, apparently due to distending the bronchioles through internal pressure. This observation provided an additional stimulus to employ positive pressure respiration in the treatment of acute pulmonary edema: we reported in a preliminary communication three cases in which a swift clearance of the moist râles in the chest took place, even in the presence of advanced circulatory deficiency. (7)

Coarctation of the Aorta

Successful closure of the ductus arteriosus in children in 1938 emboldened cardio-thoracic surgeons to eye repair of aortic coarctation as the next target. However, this operation required clamping the thoracic aorta above and below the aortic constriction long enough to perform an end-to-end anastomosis of the aorta, and the fear of ischemic paralysis in the lower half of the body held back a rush to deal with coarctation. However, in the early 1940s, Clarence Crafoord in Stockholm had a bad day in operating on a patient with a patent ductus arteriosus. The patient's ductus tore loose, leaving a gaping hole in the aorta. Crafoord had no choice but to clamp the aorta until he could sew the hole in it. The aorta was clamped almost 30 minutes but the patient recovered with no sign of paralysis of the lower extremities (8). Crafoord reasoned that, because patients with coarctation of the aorta usually have well-developed collateral circulation between the upper and the lower part of the body, he would have sufficient additional time in these patients to repair their constricted aorta. He decided it was time to go ahead, and performed two successful operations in October 1944 (9).

It was the combination of the accidental experience with the ductus and clear reasoning that led Crafoord to perform resection of the coarcted segment and end-to-end anastomosis in the successful treatment of coarctation of the aorta.

Sulfapyridine

Sulfapyridine is no longer an official drug (its only indication now is to treat dermatitis herpetiformis), but in the years 1938 to 1945, when sulfanilamide did not cure pneumococcal pneumonia and penicillin (which did) was not readily available, sulfapyridine was life saving in patients with pneumonia. I will never forget the excitement in Philadelphia in 1938 when Flippin and Pepper (10) published the first report on the use of sulfapyridine in the United States, in case after case of pneumococcal pneumonia, both of whom recovered.

It was Lionel Whitby (later Sir Lionel) in England who did the first laboratory and clinical studies of the effectiveness

of sulfapyridine against pneumococcal pneumonia. He was in the midst of testing the new drug in mice:

> Mice inoculated with pneumococci were being dosed throughout the day, but were not treated during the night. Sir Lionel had been out to a dinner party and before returning home visited the laboratory to see how the mice were getting on, and while there light heartedly gave the mice a further dose of the drug. These mice resisted the pneumococci better than any mice had ever done before. Not till about a week later did Sir Lionel realize that it was the extra dose at midnight which had been responsible for the excellent results. From that time, both mice and men were dosed day and night when under sulfonamide treatment and they benefited much more than under the old routine. (5)

Experimental Hypophysectomy

In a personal communication to W. I. B. Beveridge (5), Dr. A. V. Nalbandov told the following intriguing story of how he discovered the simple method of keeping chickens alive after the surgical removal of the pituitary gland (hypophysectomy):

> In 1940 I became interested in the effects of hypophysectomy of chickens. After I had mastered the surgical technique my birds continued to die and within a few weeks after the operation none remained alive. Neither replacement therapy nor any other precautions taken helped and I was about ready to agree with A.S. Parkes and R T. Hill who had done similar operations in England that hypophysectomized chickens simply cannot live. I resigned myself to doing a few short-term experiments and dropping the whole project when suddenly 98% of a group of hypophysectomized birds survived for 3 weeks and a great many lived for as long as 6 months. The only explanation I could find was that my surgical technique had improved with practice. At about his time, and when I was ready to start a long-term experiment, the birds again started dying and within a week both recently operated birds and those which had lived for several months, were dead. This, of course, argued against surgical proficiency. I continued with the project since I now knew that they could live under some circumstances which, however, eluded me completely. At about this time I had a second successful period during which mortality was very low. But, despite careful analysis of records (the possibility of disease and many other factors were considered and eliminated) no explanation was apparent. You can imagine how frustrating it was to be unable to take advantage of something that was obviously having a profound effect on the ability of these animals to withstand the operation. Late one night I was driving home from a party via a road which passes the laboratory. Even though it was 2 a.m. lights were burning in the animal rooms. I thought that a careless student had left them on so I stopped to turn them off. A few nights later I noted again that the lights had been left on all night. Upon enquiry it turned out that a substitute janitor, whose job it was to make sure at midnight that all the windows were closed and doors locked, preferred to leave on the lights in the animal room in order to be able to find the exit door (the light switches not being near the door). Further checking showed that the two survival periods coincided with the times when the substitute janitor was on the job. Controlled experiments soon showed that hypophysectomized chickens kept in darkness all died while chickens lighted for 2 one-hour periods nightly lived indefinitely. The explanation was that the birds in the dark do not eat and develop hypoglycaemia from which they cannot recover, while birds which are lighted eat enough to prevent hypoglycaemia. Since that time we no longer experience any trouble in maintaining hypophysectomized birds for as long as we wish.

Experimental Poliomyelitis

Landsteiner discovered poliovirus in 1909 and reported the experimental transmission of poliomyelitis to monkeys. However, a satisfactory vaccine against polio was not developed until the 1950s and early 1960s. Part of this long delay was due to a conviction that poliomyelitis could be transmitted only to monkeys and chimpanzees, and, in pre-NIH days, this limited research on experimental polio to a few well-endowed research centers that could afford to pay for monkeys. A discovery that enabled both poor and rich to work on experimentally produced polio was the finding of Armstrong in 1939 that polio could be transmitted to the cotton rat (*Sigmodon hispidus hipidus*) and from it to the white mouse (11).

Paul, in his *History of Poliomyelitis* (12), tells about Armstrong's discovery:

> I have many times tried to extract the reasons from ... Charles Armstrong which prompted him to attempt to adapt poliovirus to cotton rats instead of to mice. Rats would seem to have been a singularly unfavorable species of rodent, particularly since many a trial had shown that they are quite resistant to the commoner viral infections that attack man. ...
>
> The only satisfactory answer I could ever obtain from Dr. Armstrong was that there was currently at the NIH a colony of various species of rats being used in investigations on Weil's disease, a spirochaetal infection transmitted to man by rats. Apparently an excess supply of these rodents including a specimen of the cotton rat (*Sigmodon hispidus hispidus*) was turned over to Dr. Armstrong, who promptly tested its susceptibility to the Lansing strain of poliovirus.
>
> Armstrong's first experiments were begun in November 1937. Luck was with him on two counts: in his choice of the particular species of rat as the test animal: and in his choice of the Lansing strain, eventually identified as belonging to Type II poliovirus.

which, as it turned out later, was the type most amenable to this sort of adaptation. He began by inoculating the 19th monkey passage of Lansing virus into several species of rodents, including one cotton rat. This lone animal remained well until the 25th day, when it developed a disease resembling experimental poliomyelitis, and lo and behold, when it was sacrificed the pathological report confirmed the diagnosis. ...

This discovery, soon confirmed by others, meant that at last a strain of poliovirus was available that could be used to study the experimental disease in a far cheaper animal than the monkey. It meant neutralization tests could be done by using this stain with a sufficient number of animals to yield statistically significant results. Infinitely more important, instead of there being only a few laboratories which could afford to work with polioviruses, many could now join in the attack. In fact, Armstrong's discovery turned out to be one of those tremendously significant ones that have occasionally punctuated the history of poliomyelitis and turned it in a new direction. It suddenly accelerated progress that had only been inching along during the previous decade. A new era had begun. ...

Charles Armstrong's discovery in 1939 suddenly shed a completely new light on the behavior of poliovirus, with implications which neither he nor anyone else had appreciated or even contemplated. Not only could mice replace monkeys as the test animal in many studies of experimental poliomyelitis, but investigators could start considering the possibility that they might, after all, manipulate strains of poliovirus so as to change their virulence for humans without altering their antigenicity. As a result, such strains might be used as immunizing agents in man.

B. Chance Changed a Scientist's Goal

Penicillin

Almost everyone knows the story of the penicillium mold that floated in the breeze through an open window onto an open culture plate in Alexander Fleming's laboratory. In accepting the Nobel award in 1945, Fleming said (13):

> In my first publication I might have claimed that I had come to the conclusion, as a result of serious study of the literature and deep thought, that valuable antibacterial substances were made by moulds and that I set out to investigate the problem. That would have been untrue and I preferred to tell the truth that penicillin started as a chance observation.

And on another occasion Fleming said:

> There are thousands of different molds, and there are thousands of different bacteria, and that chance put that mold in the right spot at the right time was like winning the Irish Sweepstakes. (14)

Actually, practically the same incident happened in Tyndall's laboratory in 1877, when penicillium mold and airborne bacteria alighted on the same spot on Tyndall's culture plates and the mold mopped up the bacteria. But Tyndall was a physicist interested in, among other things, scattering of light by unseen particles floating in air: although he helped Pasteur in winning his fight against the theory of spontaneous generation, it was by using his new physical methods to identify air that was "optically pure" and air that was not.

Fleming never proved that penicillin was an antibiotic in animals or man and never purified the substance. That fell to Florey, Chain, and the Oxford group. Chance also favored them in three ways. First, they did not begin their study in the hope of finding a clinically useful antibiotic; second, they elected, for no known reason, to infect mice and not guinea pigs (they were indeed lucky because penicillin is nontoxic to mice and quite toxic to guinea pigs); and third, although they believed their stable extract to be pure penicillin, 99 per cent of the extract consisted of impurities and only 1 per cent was penicillin. (Had the combined effect of the impurities been toxic—it was *not*—it would have masked completely the safety of penicillin and might have delayed further attempts for some years [15]).

Percussion and Auscultation

Another oft-quoted example of chance is that three factors led Auenbrugger to use the technic of percussion in medicine. (1) His father was an innkeeper who regularly tapped on his barrels to learn how much was liquid and how much was air. (2) Auenbrugger was an accomplished musician with an excellent ear for pitch. (3) He chose medicine for his career instead of music or innkeeping. And two factors led Laennec to devise his stethoscope. In the introduction to the second part ("Diagnosis") of his *Treatise*, Laennec wrote:

> In 1816, I was consulted by a young woman labouring under general symptoms of diseased heart, and in whose case percussion and the application of the hand were of little avail on account of the great degree of fatness. The other method just mentioned being rendered inadmissable by the age and sex of the patient, I happened to recollect a simple and well-know fact in acoustics, and fancied at the same time, that it might be turned to some use on the present occasion. The fact I allude to is the augmented impression of sound when conveyed through certain solid bodies, as when we hear the scratch of a pin at one end of a piece of wood, on applying our ear to the other. Immediately, on this suggestion, I rolled a quire of paper into a sort of cylinder and applied one end of it to the region of the heart and the other to my ear, and was not a little surprised and pleased, to find that I could thereby perceive the action of the heart in a manner much more clear and distinct than I had ever been able to do by the immediate application of the ear. From this moment I imagined that the circumstance might furnish means for

enabling us to ascertain the character, not only of the action of the heart, but of every species of sound produced by the motion of all thoracic viscera. (16)

The Pancreas and Diabetes Mellitus

Von Mering and Minkowski, professors at the University of Strasbourg, were engaged in 1889 in studying the external secretion of the pancreas and particularly its role in digestion. As part of their research, they learned to remove the pancreas completely from dogs. A laboratory assistant noted that large numbers of flies swarmed about the urine of a dog whose pancreas had been removed and called this observation to the professors' attention. Minkowski analyzed the urine and found it loaded with sugar. It was this chance finding that led to the certain knowledge that the pancreas had multiple functions, one of which was to regulate the concentration of blood glucose.

Ergotoxine-Epinephrine Interaction

Although at first glance, this observation seemed to be only a pharmacologic curiosity, it led first to the knowledge that epinephrine had two types of actions, then to their separation by the ability of certain drugs to block what we now call α-receptors and finally to finding β-receptors and drugs that stimulate and block those. Sir Henry Dale tells how it came about (17):

> In 1904, however, at the age of 29, faced with what then seemed a rather bleak academic prospect, I accepted a research post in the Wellcome Physiological Research Laboratories, then at Herne Hill. These laboratories did a number of important services to the business of Burroughs Wellcome & Co., but they were also rather a pet project of the sole proprietor of that business, Mr. (later Sir) Henry S. Wellcome, who told me that it was his wish that research of permanent value to science might be done there. ... When I accepted the appointment, Mr. Wellcome said to me that, when I could find an opportunity for it without interfering with plans of my own, it would give him a special satisfaction if I would make an attempt to clear up the problem of ergot, the pharmacy, pharmacology and therapeutics of that drug being then in a state of obvious confusion. Pharmacological research was for me a complete novelty, and I was, frankly, not at all attracted by the prospect of making my first excursion into it on the ergot morass. ... Barger ... had already prepared from ergot a number of the substances which then figured in the pharmacological literature, with claims made for each to be ergots "active principle." I thought that I might make a beginning by testing some of these, for the kind of pharmacological activity which was within reach of my limited technical competence. So I began with their effects on the arterial blood-pressure of the anaesthetized, or, more commonly, the spinal cat. ...By one of my greatest strokes of good fortune, however, it was to give me an immediate opportunity of making a mistake of my own—a really shocking "howler." I was finishing one of these experiments on a spinal cat, to which I had given successive doses of one of Barger's ergot preparations, when a sample of dried suprarenal gland substance was delivered to me from the Burroughs Wellcome factory, with a request that I would test it for the presence of a normal proportion of adrenaline. The moment seemed opportune; a boiled extract was easily prepared, and there was a cat most suitable, as it seemed, for the required test. Successive injections of the extract elicited, to my surprise, only falls of the arterial pressure, and, with the confidence of inexperience, I condemned the sample without hesitation. And then, by another and almost incredibly fortunate coincidence, the same sequence of events was repeated in detail a week later. Again I was finishing an experiment on a spinal cat, which again had been heavily dosed with an ergot preparation, when a sample of suprarenal gland substance was again delivered for testing. Quite possibly it was the same batch again, sent to control not only the quality of the material, but also the competence of the new young pharmacologist; but that was never revealed to me. The result was, of course, the same as on the earlier occasion; but reference to my notes now raised the question whether the cat's response to adrenaline might have been so altered, by the heavy doses of ergot given in both cases, that the normal, pressor action had been reversed. It seemed unlikely, but control tests showed promptly that, in an animal not thus treated with ergot, both samples of the suprarenal material had the usual pressor action, representing a normal content of adrenaline, and then that treatment with ergot reversed this action of pure adrenaline itself.

Epinephrine and Ephedrine

The striking effects of each of these on blood pressure and on the sympathetic nervous system were first noted by chance. Sir Henry Dale (18) tells the story of how Oliver and Schäfer discovered the action of an extract from the adrenal medulla:

> Dr. George Oliver, a physician of Harrogate, employed his winter leisure in experiments on his family, using apparatus of his own devising for clinical measurements. In one such experiment he was applying an instrument for measuring the thickness of the radial artery; and, having given his young son, who deserves a special memorial, an injection of an extract of the suprarenal gland, prepared from material supplied by the local butcher, Oliver thought that he detected a contraction or, according to some who have transmitted the story, an expansion of the radial artery. Whichever it was he went up to London to tell Professor Schäfer what he thought he had observed, and found him

> engaged in an experiment in which the blood pressure of a dog was being recorded; found him, not unnaturally, incredulous about Oliver's story and very impatient at the interruption. But Oliver was in no hurry, and urged only that a dose of his suprarenal extract which he produced from his pocket, should be injected into a vein when Schäfer's own experiment was finished. And so, just to convince Oliver that it was all nonsense, Schäfer gave the injection, and then stood amazed to see the mercury mounting in the arterial manometer till the recording float was lifted almost out of the distal limb.

Ephedrine was an old Chinese herbal remedy unknown to Western medicine. In 1922-24, Carl Schmidt, then an instructor in pharmacology at the University of Pennsylvania, went to China for two years to be an associate in pharmacology at Peking Union Medical college where he worked with K. K. Chen, who had just received a Ph.D. in Physiology at Wisconsin. Although their goal was to uncover active drugs from a huge number of remedies listed in Chinese *Materia Medica*, they were both skeptical, to the point of baiting a Chinese druggist with the question, "Is there really a potent drug in this whole group of native herbs?" The druggist responded by giving them a sample of Ma Huang. The two pharmacologists put it on a shelf and went about their other studies. In 1923 they remembered the Ma Huang, made a decoction from it and injected it intravenously in an anesthetized dog still alive at the end of a student experiment. Like Schäfer some years before with adrenaline, they were amazed to observe a tremendous, long-lasting rise in systemic arterial blood pressure (19). The Chinese druggist's Ma Huang put Chen into a long and productive career of pharmacology and for 34 years he directed pharmacological research at Eli Lilly & Co.

[To be continued on the following pages.]

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REFERENCES

1. Lamb, Charles: A dissertation upon roast pig, in *The Essays of Elia*, orig. ed. 1823, reprinted 1892, Little, Brown Co., Boston.
2. Graham, E. A.: The story of the development of cholecystography, Am J Surg, 1931, 12, 330-335.
3. Koch, R.: Die Aetiologie der Tuberculose, Berlin Klin Wochenschr, 1882, 19, 221-230. English translation, deRouville, W., Med Classics, 1937-1938, 2, 853-880.
4. Gibson, W. C.: Young Endeavour. Contributions to Science by Medical Students of the Past Four Centuries, Charles C Thomas, Springfield, Ill., 1958.
5. Beveridge, W. I. B.: The Art of Scientific Investigation, Random House, New York, 1950.
6. Barach, A. L.: in Who's Who in America, 1974-1975, ed. 38, vol. 1, p. 152.
7. Barach, A. L., Martin, J., and Eckman, M.: Positive pressure respiration and its application to the treatment of acute pulmonary edema, Ann Intern Med, 1938, 12, 754-795.
8. Johnson, S. L.: The History of Cardiac Surgery 1896-1955, Johns Hopkins Press, Baltimore, Md., 1970.
9. Crafoord, C., and Nylin, G.: Congenital coarctation of the aorta and its surgical treatment, J Thorac Surg, 1945, 14, 347-361.
10. Flippin, H. F., and Pepper, D. S.: The use of 2 (*p*-aminobenzenesulphonamido) pyridine in the treatment of pneumonia. A preliminary report, Am J Med Sci, N. S., 1938, 196, 509-513.
11. Paul, J. R.: A History of Poliomyelitis, Yale University Press, New Haven, Conn., 1971.
12. Armstrong, C.: The experimental transmission of poliomyelitis to the eastern cotton rat, *Sigmodon hispidus hispidus*, USPHS Pub Health Rep. 1939, 54, 1719-1721.
13. Fleming, A.: Penicillin, in *Nobel Lectures, Physiology or Medicine*, 1942-1962, Elsevier, Amsterdam, 1964.
14. Austin, J. H.: The roots of serendipity, Sat Rev World, November 1974, pp. 60-64.
15. Taton, R.: Reason and Chance in Scientific Discovery, A. J. Pomerans, trans., Hutchinson Scientific and Technical, London, 1957.
16. Willius, F. A., and Keys, T. E.: Classics of Cardiology, vol. 1, Dover Publications, New York, 1941, p. 326.
17. Dale, H. H.: Adventures in Physiology with Excursions into Autopharmacology, Pergamon Press, London, 1953.
18. Dale, H.: Accident and opportunism in medical research, Br Med J, 1948, 2, 451-455.
19. Chen, K. K., and Schmidt, C. F.: The action of ephedrine, the active principle of the Chinese drug, Ma Huang, J Pharmacol Exp Ther, 1924, 24, 339-357.

Part II

In Part I of "Roast Pig and Scientific Discovery" (American Review of Respiratory Disease, May 1977), I gave a classic instance of Chance, or Serendipity, as related by Charles Lamb in his "Dissertation upon Roast Pig." In this essay, Lamb tells how many centuries ago Bo-Bo, the Chinese swine-herd's son, stumbled upon the delicacy of roast pork when he accidentally burned down his father's house and barn and in the process roasted ("burnt") nine newly farrowed pigs. I then gave (A) eight examples in which chance speeded or completed a scientist's ongoing work and (B) five examples in which chance changed the direction of a scientist's work and pointed him toward a new goal. In Part II, I will give more examples of a change in direction of a scientist's work that resulted from chance, and speculate on the role of chance in speeding the advance of science.

Anaphylaxis

"Phylaxis," a word seldom used, comes from the Greek, meaning "protection." "Anaphylaxis" means, strictly speaking "*without* protection" and, therefore, hypersensitive; in its usual context, it means that the first injection of a substance, instead of conferring protection against a second injection, makes the organism hypersensitive. Charles Richet, Nobel Laureate in Physiology, 1913, tells how he discovered the phenomenon (20):

> These are the circumstances under which I first observed this phenomenon. You will allow me to go into some details on the origins. You will find that it is by no means the result of profound thought but a simple observation, almost a fortuitous one; so that my merit has only been in letting myself see the facts which were plain before me.
>
> In tropical waters, Coelenterata are to be found floating on the surface, also known as Physalia (Portuguese galleys). The basic structure of these creatures is a pocket filled with air so that they can float like a bladder. A bucco-anal cavity is subjoined to this pocket, with very long tentacles which hang in the water. These feelers sometimes run to two or three meters long and are equipped with small devices which adhere like sucking cups to objects encountered. Within each of these innumerable suction-cups is a pin-point which drives into the foreign body that is being touched. At the same time, this pin-point causes penetration of a subtle but strong poison, which is contained in the tentacles, so that contact with a feeler of the Physalia is tantamount to a multiple injection of poison. On touching a Physalia an acute sensation of pain is felt immediately, due to the penetration of this liquid venom. This is similar in relative intensity to a swimmer's mishap when he bumps into a jelly-fish in the water.
>
> During a cruise on the yacht of Prince Albert of Monaco, the Prince advised me to study Physalia poison, together with our friends Georges Richard and Paul Portier. We found that it is easily dissolved in glycerol and that by injecting this glycerol solution, the symptoms of Physalia poisoning are reproduced.
>
> When I came back to France and had no more Physalia to study, I hit upon the idea of making a comparative study of the tentacles of the Actinia (*Actinia equina, Anemone sulcata*) which can be obtained in large quantities, for Actinia abound on all the rocky shores of Europe.
>
> Now Actinia tentacles, treated with glycerol, give off their poison into the glycerol and the extract is toxic. I therefore set about finding how toxic it was, with Portier. This was quite difficult to do, as it is a slowly acting poison and three or four days must elapse before it can be known if the dose be fatal or not. I was using a solution of one kilo of glycerol to one kilo of tentacles. The lethal dose was of the order of 0.1 liquid per kilo live weight of subject.
>
> *But certain of the dogs survived, either because the dose was not strong enough or for some other reason. At the end of two, three or four weeks, as they seemed normal I made use of them for a new experiment* (italics added).
>
> An unexpected phenomenon arose, which we thought extraordinary. A dog when injected previously even with the smallest dose, say of 0.005 liquid per kilo, immediately showed serious symptoms: vomiting blood diarrhoea, syncope, unconsciousness, asphyxia and death. This basic experiment was repeated at various times and by 1902 we were able to state three main factors which are the corner-stone of the history of anaphylaxis: (1) a subject that had a previous injection is far more sensitive than a new subject; (2) that the symptoms characteristic of the second injection, namely swift and total depression of the nervous system, do not in any way resemble the symptoms characterizing the first injection; (3) a three or four week period must elapse before the anaphylactic state results. This is the period of incubation.

It is said that lightning never strikes twice in the same place, but read how Sir Henry Dale discovered in 1913 that anaphylactic contraction of smooth muscle resulted from the formation of cell-fixed antibodies (21):

> Then I had another stroke of luck. I was studying a rather weak activity of a similar kind which fresh blood serum exhibited when it was applied to strips of involuntary muscle taken from a dead guinea-pig, and I suddenly encountered a strip of this tissue from one particular guinea-pig which responded with a contraction of peculiar violence when it was treated with a mere trace of horse serum, though it behaved quite normally in the presence of blood serum from other animals—cat, dog, rabbit, sheep, or man. And it occurred to me

> that many guinea-pigs in that laboratory were used for testing the strength of antitoxic horse serum, and that an economically minded colleague might have provided me with a survivor from such a test. The verification of that suspicion gave us a new idea about the meaning of the anaphylactic or allergic condition.

Because Dale worked in the days before there were large-scale grants, he and other scientists often used an animal that survived one experiment as the subject of another, a necessary but risky practice; in this case the twice-used guinea pig received horse serum each time—first to standardize an antitoxin and second to test responses of "normal" uterine smooth muscle to horse serum.

The Function of the Carotid Body

Although DeCastro, on the basis of his brilliant neurohistologic studies, deduced in 1928 that the carotid body must be a chemoreceptor organ (one that "tastes" the blood and reports on its chemical composition to the brain), it remained for Heymans and his associates to demonstrate this concept experimentally. Eric Neil, a close associate of Heymans, states that although DeCastro wrote in French and Heymans was a French-speaking Belgian, Heymans made his 1930-31 discovery without knowing of DeCastro's 1928 work. This is how Heymans made his discovery, according to Neil (22):

> At the end of a long experimental day in which he had been examining the effects of drugs on *baroreceptor* reflexes, the dog was still in good experimental condition, with one carotid bifurcation denervated and the other bifurcation still innervated by its sinus nerve. He remembered a saying of his father, which, paraphrased, was "At the end of a good experiment which has given clear results, if the animal is in satisfactory experimental condition, try an imaginative or even a facetious experiment." He decided to test the effect of injection of sodium cyanide into the carotid artery on each side. The drug was known to cause hyperpnoea and was believed to stimulate the medullary respiratory centres directly. On injecting cyanide into the carotid which supplied the innervated bifurcation the usual hyperpnoea resulted, but when the injection was made on the denervated side no respiratory response occurred. Repeating the dual procedure several times he obtained the same results. He and his colleagues realized that they had proved that sodium cyanide provoked a chemical reflex and that the old hypothesis of a central action was wrong. The subsequent days were spent in repeating the experiment in newly-prepared animals and confirming their findings. The first demonstration of the carotid chemoreflex aroused by histotoxic anoxia was made in this manner. Important though it was, the full development of our understanding of a possible *physiological* role of the carotid chemoreflexes in monitoring or in affecting the breathing could hardly have occurred so quickly if Heymans had not already been armed with the formidable technique required for perfusing the carotid bifurcation (using either a donor dog or a Dale-Schuster pump) with blood of altered chemical composition [as Heymans had done before in testing for chemosensitivity in the "cardio-aortic" regions].

Development of Collateral Circulation

John Kobler, in his biography of John Hunter (23), tells how, in 1785, that remarkable man discovered the concept and fact of collateral circulation:

> Most varieties of stag shed their antlers and grow a new pair every year. Among the pending investigations on John's crowded agenda was the mode of this growth. Through what channels did the new cartilage derive its nutriment? Probably, John speculated, through the two carotid arteries running up the sides of the animal's neck.
>
> Richmond Park, a crown property of almost twenty-five hundred acres lying on the south bank of the Thames, seven miles from the center of London, had originally been enclosed by Charles I as a deer-hunting preserve, and though it had since been opened to the public, deer by the hundreds still roamed its thick groves. One of the privileges George III had accorded John was that of drawing upon the deer herds for experimental material, and in July of that year the surgeon availed himself of it. He had park wardens snare a young stag. He then laid bare one of the carotid arteries and tied it with surgical thread.
>
> When he returned to examine the stag a few days later, it was as he expected: the antler corresponding to the ligated artery had stopped growing and felt cold to the touch. Clearly, it was receiving no nutriment. Would it be shed sooner than usual? On re-examining it a week later, after the wound around the ligature had healed he saw, to his astonishment, that the antler was warm again and had resumed growing.
>
> Could he have failed to ligate it securely? Was blood somehow still passing through it? He ordered the stag killed and brought to Leicester Square, where he dissected the area at the base of the antlers. He satisfied himself that he had not bungled the ligature. Yet a curious change had taken place. Some of the smaller arterial branches, above and below the ligature, were enlarged. It was through this mysteriously arisen auxiliary system, John reasoned, that blood must have been supplied to the antlers.
>
> His swift conclusion was, in the words of Sir James Paget, one of the great pathologists of the nineteenth century, "a signal instance of the living force there is in facts when they are stored in a thoughtful mind." From the single observation of the altered blood ves-

sels John deduced the entire principle of collateral circulation. According to this principle, the smaller, tributary arteries will, under "the stimulus of necessity," to use John's typically vitalist phrase, assume the functions of the larger. To verify this, John had Everard Home ligate the femoral artery of a dog and, later, dissect the leg. Home reported the same findings. Here was further confirmation of John's belief in the body's ability to throw up its own defenses.

Shortly thereafter, Hunter, instead of amputating the leg of a patient with a popliteal aneurysm, as was then the custom, simply ligated the artery above the aneurysm and allowed collateral circulation to provide adequate blood flow to save the limb.

Immunization

Jenner in 1798 had shown that inoculating a subject with cowpox produced a rather mild disease that then protected the individual against fatal or disfiguring smallpox. However, the idea of deliberately attenuating *virulent* bacteria and then using these to develop protection against disease and to prevent epidemics required first the discovery of the bacterial cause of many infectious diseases and then the genius of Louis Pasteur. Pasteur had been assigned the task of doing something about cholera in fowl, which was devastating the poultry farms in France. Beveridge (24) tells how Pasteur hit on the new concept:

> Pasteur's researches on fowl cholera were interrupted by the vacation, and when he resumed he encountered an unexpected obstacle. Nearly all the cultures had become sterile. He attempted to revive them by sub-inoculation into broth and injection into fowls. Most of the subcultures failed to grow and the birds were not affected, so he was about to discard everything and start afresh when he had the inspiration of re-inoculating the same fowls with a fresh culture. His colleague Declaux relates:
>
> "To the surprise of all, and perhaps even of Pasteur, who was not expecting such success, nearly all these fowl withstood the inoculation, although fresh fowl succumbed after the usual incubation period."
>
> This resulted in the recognition of the principle of immunisation with attenuated pathogens.

ANTU—A Rat Poison

It was Curt Richter, Professor of Psychobiology at Johns Hopkins University, who discovered a powerful poison, selective for Norway rats, at a time when it was needed badly. What does psychobiology have to do with rat poison? Absolutely nothing. Richter was interested in studying taste and the ability of animals to select a proper diet by using their sense of taste. Dr Richter tells how studies on taste led to a rat poison (25):

> In 1931 Dr. Herbert Fox, a research chemist at du Pont, observed that as this chemical [phenyl thiourea], in the form of fine dust, was blown through his laboratory, some fellow-workers complained of a very bitter taste while most of them denied tasting anything at all. In testing a large number of persons, Fox found that although about 85 per cent could not taste this compound, even in large amounts, about 15 per cent found it extremely bitter. ...
>
> In 1939 this substance became of special interest to me in relation to results of my dietary self-selection studies, which showed that the rat has an extraordinary ability to select beneficial substances and avoid harmful ones. These studies demonstrated that the rat's appetite is a good guide to its nutritional needs; that in fact it is reliable enough to use in determining nutritive values of various food-stuffs; that it helps the rat to avoid harmful or non-nutritive substances—which is of particular importance in view of its inability to vomit. Results of these studies indicated that taste of food-stuffs—natural or chemically purified—plays an important part in dietary selections, determining chiefly whether or not an animal will ingest a substance. It naturally interested me to determine the extent to which observations on the role played by taste in dietary selections in rats can be transferred to man—whether man and rats have similar taste abilities.
>
> Thus, when I first heard that phenyl thiourea has such a bitter taste to some people while having for others no taste at all, I wondered whether likewise some rats would taste it and others not. Ability to taste it was tested in a simple experiment. A minute amount of phenyl thiourea powder—as much as can be put on the small end of a toothpick—was placed on the tongues of six rats. The rats were then watched for signs of distaste—attempts to get rid of the powder with their paws or tongues. After watching for over half an hour, I decided that even if they could taste it they did not find it very bitter. To my great surprise the next morning all six rats were dead. They were found to have died of massive pulmonary edema and pleural effusion. Their chests and lungs were filled with fluid. Later, systematic tests showed that as little as 1-2 milligrams sufficed to kill a rat, and that when phenyl thiourea was mixed in food in small amounts, 1-2 per cent, our laboratory rats ate it freely and died. Thus it was demonstrated for the first time that phenyl thiourea is highly toxic to rats, and that rats will eat it in toxic amounts.

Richter had set out to prove that nature had provided rats with taste receptors that enabled them unerringly to select the good and reject the bad—but with Norway rats, nature instead gave them receptors that allowed them to enjoy a lethal man-made poison. Richter realized the potential value of a rat poison and directed the secret wartime development and large

scale testing of a derivative (alpha naphthyl thiourea: ANTU). Incidentally, he also found that chronic administration of phenyl thiourea blocked the formation of the thyroid hormone; Astwood followed up this work and discovered the clinical usefulness of antithyroid drugs in 1943 (26).

Radioimmune Assay

This new analytic procedure has permitted hospital laboratories and research scientists to make highly specific and sensitive measurements to many hormones such as insulin, growth hormone, ACTH, and parathyroid hormone. Berson and Yalow discovered it by chance (27):

> About 15 years ago we were interested in evaluating whether diabetics destroyed insulin more rapidly or more slowly than normal subjects. It had been recognized that not all diabetes is associated with an absolute deficiency of insulin, and Dr. Arthur Mirsky ... suggested that this phenomenon might be traceable to an overly active insulin-destroying enzyme, insulinase. To test this hypothesis, we injected radiolabeled insulin intravenously and determined the rates of disappearance and degradation of the tagged hormone. Surprisingly, we found that insulin did not disappear more rapidly from the circulation of the diabetics but was retained in the plasma for longer periods than in the normal subjects. However, it turned out that this slow disappearance rate was not directly related to the presence of diabetes. Rather, it was because the diabetics had anti-insulin antibodies, which complexed with the hormone in the plasma, thus preventing the insulin molecule from passing through the capillary walls. ... During the course of these studies we found it convenient to use radio labeled insulin as a tracer, giving increasing amounts of unlabeled hormone in order to quantitate the insulin-binding capacity of the plasma antibodies. It was evident that the labeled and unlabeled insulins were competing for antibody combining sites and that the extent of this competition could serve as the basis for an assay of insulin.

Motion Sickness

Gay and Carliner were allergists at the Johns Hopkins Hospital and, naturally, in 1947, were interested in using old and new antihistaminic drugs to treat their allergic patients. That year Searle & Co. sent them a new drug, Dramamine®, for clinical investigation of its value in controlling hay fever and hives. The allergists gave the new drug to a number of patients, one of whom incidentally had suffered all her life from car sickness. During an interview at the hospital, she volunteered the information that since she had been taking the new drug, she had no further difficulty with motion sickness. Dr. Gay immediately realized the importance of her observation and switched her back and forth between Dramamine and a placebo of sugar: after Dramamine she never had car sickness, but after the placebo she always had severe sickness. Gay and Carliner (28) then found other victims of car sickness and airsickness and these were, without exception, completely freed of discomfort, provided the drug was taken just before exposure to the motion that provoked the illness.

The new drug had a large-scale clinical trial by the Armed Forces because General Omar Bradley recognized the military value of such a drug in landing operations such as that in Normandy in 1945. Soon "Operation Seasick" had Dr. Gay aboard a troopship with 1,500 soldiers for 12 days in a rough North Atlantic; the study showed that drugs could be effective both in preventing and relieving motion sickness.

Catheterization of Coronary Arteries and Coronary Sinus

Physiologists had for many decades perfused the coronary arteries of animals with Ringer solution, modified Ringer solutions, or blood (even hypoxemic blood) but were apprehensive about sending a block of an unoxygenated foreign fluid through the coronary circulation for fear of inducing serious arrhythmias. Yet successful coronary arteriography required flow of a highly concentrated, radiopaque solution through the coronary circulation. How did visualization of the coronary arteries become a diagnostic test? Litwak (29) tells this story:

> In 1958 an event transpired in Cleveland which was destined to have virtually unparalleled influence on medicine's understanding of coronary artery disease. F. Mason Sones, Jr. and his colleagues at the Cleveland Clinic were studying a young adult and had withdrawn their catheter from the left ventricle into the supravalvar area in preparation for an aortagram. Their equipment at that time did not allow them to precisely visualize the catheter tip immediately prior to injection of the contrast material. The usual dose of 35 mL of a 90 per cent diatrizoate compound was injected and, to Sones' horror, the right coronary artery and its distal branches were clearly visualized. Obviously, the catheter had accidentally entered the right coronary orifice and dye injected. The patient had remained stable throughout the entire procedure. That fortuitous event taught Sones that, contrary to views held at that time concerning electrical instability of the heart, non-oxygen carrying fluid could be injected into a major coronary artery without untoward event. Secondly, Sones realized that with proper equipment he could reduce the coronary artery injectate by ten-fold and he would then be able to sequentially study the entire coronary circulation of man and visualize vessels with a dimension of 100 microns or larger.

Eller writes of this:

> The ... introduction of selective coronary arteriography in 1958 did ... much more than improve the

> diagnosis of ischemic heart disease. Figuratively speaking, Sones' catheter pried open the lid of a veritable treasure chest and brought forth the present era of revascularization surgery. His technic did provide for accurate diagnosis in coronary arterial disease but, more important, it defined the needs of the individual patient. For these reasons alone, coronary arteriography was a monumental contribution ...

The first catheterization of the coronary sinus in man was also accidental. After Cournand and Ranges introduced the technique of cardiac catheterization to cardiologists in 1941, several teams began to use the new method to measure cardiac output in man, using the Fick principle. The latter required knowing the O_2 content of samples of systemic arterial and mixed venous blood, drawn simultaneously, to determine the difference between the two. Mixed venous blood could at last be obtained from a catheter properly placed in the patients right heart. The main problem that plagued workers in the early 1940s was that blood drawn through the catheter sometimes didn't seem to be well-mixed venous blood.

Cournand, about 1941, attempting to catheterize the right ventricle, obtained a sample of blood with a lower oxygen content than right artrial blood. Because the fluoroscopic picture showed that the catheter tip was misplaced and was probably in the coronary sinus (by mere chance), and Cournand was concerned about possible damage to the lining of the sinus, he hastily withdrew the catheter.

Stead and co-workers had trouble with 3 patients because the sample of blood from the right heart had a very low O_2 content; they concluded that the catheter must have slipped into the coronary sinus, discarded the data, and went on to study better-behaved patients (30).

Sosman, a radiologist in Boston who worked with Dexter on cardiac catheterization, listed among his "failures and errors" (31) unexpected locations of the catheter tip and published in his figure 3C a roentgenogram showing a catheter tip in the coronary venous sinus; he confirmed its location by measuring the O_2 saturation of blood drawn through it (only 25 per cent instead of the usual 75 per cent in truly mixed venous blood).

Bing and his associates wrote in 1947, "When the catheter is in the coronary sinus, it is seen curved upward toward the base of the heart. ... In the first five cases, intubation of the theses vessels was fortuitous. ... In the remaining four cases, catheterization of the sinus was carried out deliberately. ... The difference between the oxygen contents of peripheral arterial blood (and hence of coronary arterial blood), and of coronary venous blood varied from 11.3 to 18.7 vol %, while the total systemic arteriovenous oxygen difference varied from 2.8 to 7.3 vol %" (32a). Bing, a pioneer in using the catheter to diagnose, with precision, congenital heart lesions in children, quickly changed directions and now pioneered in the new, richly rewarding field of coronary blood flow and cardiac metabolism in man (32b).

Probenecid

The discovery of penicillin as a powerful, relatively nontoxic antimicrobial drug was made in 1941. It was difficult to produce in large quantities, and, to make matters worse, much of the penicillin administered to patients was excreted rapidly by their renal tubules and ran out in the urine so that it required huge doses of penicillin to maintain an effective concentration of it in blood. Beyer and Sprague at Sharp & Dohme hit upon the idea of using paraaminohippurate, also secreted by the renal tubules, to block the outpouring of penicillin. It worked but took large amounts. They synthesized other compounds that might be even more effective in lower doses. The first of these was carinamide, better than the hippurate, but not good enough. The next was probenecid, considerably better at blocking penicillin excretion; but now, ironically for them, there was no market for such a drug. The U.S. Office of Scientific Research and Development (OSRD) had given top priority to the mass production of penicillin, initially for the British troops in World War II and then for American soldiers as well, and soon there was enough to go around, without blocking urinary excretion of penicillin.

However, in 1950, Berliner and his associates found the renal tubular mechanism for excretion of urates in man (33), and during the next year, Bishop, Rand, and Talbott found that probenecid greatly increased uric acid secretion in normal man and in a patient with gout (34). So a drug designed to keep penicillin in the body turned out to be useful in getting uric acid out of the body and so an effective treatment for human gout.

Oral Diuretics

The first powerful oral diuretic, chlorothiazide, resulted from careful bedside observation, basic research, and chance. The careful bedside observation was that of Southworth, who noted in 1937 that patients taking then-new sulfanilamide had acidosis, and that volunteers taking sulfanilamide had a marked increase in urine volume and in their excretion of sodium and potassium. The basic research was the first discovery by Roughton of a new enzyme, carbonic anhydrase, in red blood cells, that tremendously speeds the reaction: $CO_2 + H_2O \Leftrightarrow H_2CO_3 \Leftrightarrow H^+ + HCO_3^-$; second, Davenport's finding that this enzyme is present in stomach and kidney, both acid-producing organs: third, the work of Pitts and Alexander showing that acidification of urine in the renal tubules requires carbonic anhydrase.

Beyer, at Merck, Sharp & Dohme, had been trying, by means of drugs, to prevent loss of valuable penicillin in urine (see *Probenecid*). When the props were knocked out from under the program by mass production in the United States, he changed direction and started to devise drugs that increased renal excretion of sodium and water, instead of blocking urinary penicillin. The work of Davenport and Pitts led Beyer

to investigate a large group of sulfanilamide derivatives to find a more potent and less toxic inhibitor of carbonic anhydrase, believing that it would be a more potent diuretic; chlorothiazide was the result. Chance entered this story in three ways: (1) the OSRD quickly produced penicillin in large quantities, making Beyer's conservation program unnecessary. (2) Although chlorothiazide is both a carbonic anhydrase inhibitor and a potent diuretic, its diuretic effect was found to be unrelated to its action on carbonic anhydrase. (3) Beyer wanted a diuretic to treat patients with congestive heart failure; because of a long-known association between salt and hypertension, Beyer's diuretic soon became an important antihypertensive drug. It is rare, except in chemotherapy, that one substance becomes the drug of choice in treating two important diseases (congestive heart failure and essential hypertension). Its discovery soon led to other types of oral diuretics, some of which, such as ethacrynic acid and furosemide, either do not inhibit carbonic anhydrase at all, or at most have a very weak action on the enzyme.

Triamterine, another oral diuretic, was also discovered by chance. Some years ago Lettré noted that a particular benzoisoalloxazine specifically inhibited certain cancer cells *in vitro*. Haddow (35) tried to confirm this. He couldn't, but found something totally unrelated; an alloxazine compound similar to Lettré's but it colored the hair of albino rats because its alloxazine penetrated into growing hair. Haddow was curious to learn whether a naturally occurring pigment such as xanthopterin (which occurs in the wings of butterflies and is related to folic acid) could also cause a color change in the fur of albino rats; it did not.

So far the story is pretty far removed from the kidneys or oral diuretics or triamterine itself. But Haddow examined the kidneys of the rats that he treated with xanthopterin and found that they were hypertrophied, that the hypertrophy started almost at once after injection of xanthopterin, and that the growth was due to a great outburst of mitotic activity in the renal tubules. This was a most unusual effect of a drug, but one that did not lend itself to clinical use because the xanthopterin was excreted in the tubules and formed crystals there.

But now the direction of Haddow's research changed to look for a chemical with a xanthopterin-like effect on tubules, but one that didn't form crystals that blocked the tubule. The right compound triamterine, came from an unexpected quarter—a study of agents that were carcinogenic. So an initial chance observation on cancer-inhibiting agents and an unexpected bonus in a later study of cancer-inducing agents led to a valuable oral diuretic agent.

Fetal Respiration

In 1936, Marshall and Rosenfeld at Johns Hopkins University noted that sodium cyanide was a good respiratory stimulant, acting reflexly through the newly discovered carotid chemoreceptors. However, because its action was too brief to be of much help in overcoming respiratory depression, they reasoned that a compound that liberated cyanide slowly into the bloodstream and over a long period might be worth studying. They decided to test pyruvic acid cyanohydrin. But the next step was to find a test animal—one that was completely apneic for long periods but still alive. Because everyone knew that the fetus *in utero* never breathed, they settled on fetal apnea as a good baseline for testing the effectiveness of a respiratory stimulant with a prolonged effect. To their amazement they found that full-term fetuses of rabbits, cats, and guinea pigs all made active, regular, and frequent respiratory movements. The problem then changed from the study of a new drug (cyanohydrin) to "direct observation of intrauterine respiratory movements of the fetus and the role of carbon dioxide and oxygen in their regulation" (36).

Alloxan and Experimental Diabetes

Shaw Dunn was not the first to describe acute renal failure as a sequela of crush injury, but he was the first to demonstrate that the renal injury was restricted to the ascending limbs of Henle's loops and second convoluted tubules of the kidney. He became interested in whether crush of skeletal muscles releases toxic factors, such as uric acid or phosphoric acid, that are responsible for the renal damage. In testing a series of uric acid derivatives, he found that alloxan (the ureide of mesoxalic acid) produced selective damage to the same renal tubules. However, the dose of alloxan required to produce this lesion killed many of the animals within a day or two; they had distinctive symptoms before death but they were not attributable to renal disease. At this point Dunn turned aside from the kidneys to explore the cause of these symptoms, since no one had ever studied the pharmacologic or toxic effects of alloxan. He came up with the remarkable finding that alloxan caused selective necrosis of the insulin-producing islets of Langerhans in the rabbit pancreas and left the other endocrine glands untouched (37). An investigation into the cause of renal failure in crush injury thus led Dunn to find a substance capable of producing experimental diabetes mellitus. Since then, alloxan has also been found to produce pulmonary edema in cats and dogs and so has provided a tool for studying the effects of increased pulmonary capillary permeability.

Isoniazid, an Antituberculosis Drug

In 1945, Ernest Huant had been in the habit of administering what he called "P. P. (pellegra preventing) vitamin" or nicotinamide to patients undergoing radiation therapy to lessen post-radiation nausea and vomiting and to improve tolerance of the skin to x-rays. Although the radiation was directed primarily against tumors, during the course of this work Huant noted clearing of densities in the chest films of certain patients who also had pulmonary tuberculosis. "With all reservations," he cautiously described his clinical findings with nicotinamide

and tuberculosis in the Gazette des Hôpitaux, and urged specialists in tuberculosis to test his findings and determine their utility (38). I don't believe that this observation changed the direction of Huant's studies, but it certainly changed that of physicians interested in treating tuberculosis.

That same year Vital Chorine indicated that he had been studying the influence of various vitamins on experimental leprosy. He admitted his surprise at the finding that large doses of nicotinamide protected against the disease in rats. Because of the relationship between the bacillus of leprosy and that of tuberculosis, Chorine attempted a similar experiment with a human strain of the tubercle bacillus and found that large doses of nicotinamide completely prevented development of tuberculosis in guinea pigs (39). Soon thereafter, many derivatives of nicotinamide were tested, and isoniazid was found.

Beri-Beri

Beri-beri, a severe polyneuritis, was first described more than 1,300 years ago in China. The ravages of beri-beri in the Dutch Indies in the late nineteenth century led the Dutch government to appoint a special commission to study the disease on the spot. The new science of bacteriology and the almost overnight explanation of many mysterious diseases as germ-induced led the commission to look for a specific bacterial cause of beri-beri. A disease suddenly afflicted chickens near the laboratory in Java and because in many respects it closely resembled beri-beri in man, these chickens seemed to be heaven-sent to help Eijkman find the cause of beri-beri.

Christiaan Eijkman in his Nobel Lecture in 1929 tells the story (40):

> Attempts to induce the infection with material from affected birds or from birds which had died of the disease were inconclusive since all the chickens, even those kept separate as controls, were affected. No specific micro-organism or any higher parasite was found.
>
> Then suddenly the disease cleared up and we were unable to continue our investigations. The affected chickens recovered and there were no new cases. Fortunately suspicion fell on the food, and rightly so, as it very soon turned out.
>
> The laboratory was still housed provisionally and in a very makeshift manner at the military hospital, although it was administered by the civilian authorities. The laboratory keeper—as I afterwards discovered—had for the sake of economy fed the chickens on cooked rice which he had obtained from the hospital kitchen. Then the cook was replaced and his successor refused to allow military rice to be taken for civilian chickens. Thus, the chickens were fed on polished rice from 17th June to 27th November only. And the disease broke out on 10th July and cleared up during the last days of November.
>
> Deliberate feeding experiments were then conducted in order to check more thoroughly whether or not the probable connection between diet and the disease actually existed. It was found for certain that the polyneuritis was due to the diet of cooked rice. The chickens were attacked by the disease after 3-4 weeks, and in many cases somewhat later, whereas the controls which were fed on unpolished rice remained healthy. In many cases birds suffering from the disease could be cured by a suitable alteration in diet.

And so arose the concept that the disease was caused by the *absence* of something (later named a vitamin and still later, thiamin) rather than by the *presence* of something (bacteria or their toxins).

Some Other Chance Discoveries

This is already a long list, without repeating the stories of some chance discoveries that I've mentioned in previous Retrospectroscopes (e.g., McLean's discovery of heparin while he was looking for a *coagulant* (41); Ringer's accidental discovery of the role of CA^{2+} and K^{+} in regulating myocardial performance (41); the accidental discovery of anesthetic effects of ether by Morton and by Long, and of nitrous oxide by Wells (42); the chance discovery of a new mercurial diuretic by Vogl, who really wanted an antisyphilitic drug (43); the circumstances that led Jacobson to use microvascular surgical technics (41); Chargaff's finding of heparin-*antagonist* while designing a compound to *prolong* its effect (41); Roentgen's discovery of x-rays (44); and Heyrovsky's turning a routine problem into the science of polarography (45).

And some chance discoveries are too well known to be repeated (e.g., Galvani's discovery of "animal electricity," Volta's creation of the "Voltaic pile" or battery, and the accidental discharge of a shotgun that gave William Beaumont the chance to study gastric physiology by direct vision in his patient, Alexis St. Martin).

The list would be longer yet if I mentioned some oft-quoted chance discoveries that sound authentic but may well be apocryphal: e.g., that a Smith, Kline and French chemist found that his precious, newly synthesized sympathomimetic crystals "vanished" when he went out to lunch and only later realized that his new compound Benzerdrine®, was volatile; that the Hungarian government forced vintners to add phenolphthalein, an indicator, to their cheap white wines to distinguish them from genu-wines, until an epidemic of diarrhea followed and a new laxative was born; that a University of Illinois chemistry student discovered the cyclamate, sucaryl, when he accidentally put his cigarette first on some chemicals on a bench top and then between his lips; that copper and lime, now known as Bordeaux mixture and a commercially important fungicide for fruit trees and vines, was first sprayed on stakes in vineyards only to frighten away pilferers; and that Ramon discovered by chance that formalin can weaken or eliminate the toxicity of toxins without diminishing their antigenicity (all he wanted to do was use formalin to preserve the toxins).

Comments on Chance

I've not become involved in a massive research effort to determine how often chance has played an appreciable, important, or essential role in major discoveries in biomedical science. A skillful investigative reporter or private eye might know how to get the evidence, but I don't. Even a little gentle probing has taught me that most scientists don't like to be regarded as *discoverers*, but rather as *scientists* who have meticulously and logically planned each step in a direct line leading from ignorance to full knowledge. Few "tell it like it was" in their scientific writing, and editors of journals probably delete, as unscientific, most of the "chance" story that authors do put in their manuscripts. However, the Retrospectroscope shows that some scientists in their initial reports do acknowledge their indebtedness to chance and many more do so later in life when the highest honors have assured them of a place in Science's Hall of Fame. These late-in-life reports lead me to believe that chance is a pretty important element in scientific advance.

If it is, how might this affect our attitude toward the support of science and scientists? Two extreme views will surely come to some minds: (1) Since chance is an important factor in discovery and since chance is really finding things by bumbling and stumbling, science has no need for highly intelligent, superbly trained men and women who proceed carefully and doggedly step by step toward a logical goal. (2) As a corollary of the first, what science really needs is a large corps of scientists in motion who bounce from project to project (as do molecules from other molecules in random motion) and so increase tremendously the number of fortuitous observations and the likelihood of a great discovery.

I'd rather train my Retrospectroscope in several different directions. First, let's look at the word that Horace Walpole coined: serendipity. The two dictionaries on my desk have changed Walpole's definition to "an apparent aptitude for making discoveries accidentally" (Webster's New World) and "the faculty for making desirable discoveries by accident" (Random House). But that was *not* what Walpole said, which was "making discoveries, by accidents and sagacity, of things which they were not in quest of" (46). The key words (omitted in recent years) are "and sagacity." Webster's New World defines *sagacity* as "penetrating intelligence, keen perception and sound judgment" and Random House as "acuteness of mental discernment and soundness of judgment."

Now let's look at Pasteur, who said much the same in the mid-1800s when he wrote: "Dans les champs de l'observation, le hasard ne favorise que les esprits prepares," translated freely as "Chance favors only the prepared mind." And let's look at Joseph Henry, America's great physicist, who said the same thing some years before Pasteur when he commented, "The seeds of great discoveries are constantly floating around us, but they only take root in minds well prepared to receive them."

And in this century, let's look in on Winston Churchill, who commented, sagaciously, "Men occasionally stumble across the truth but most of them pick themselves up and hurry off as if nothing had happened."

It seems that many discoveries, either clinical or nonclinical, are made—and then developed in different directions—by individuals who not only have prepared minds, but are willing to change the direction of their effort, not daily or weekly, but when a new observation—possibly a chance observation—appears to be far more important than the problem before them. This requires three additional qualities besides the ability to observe what chance has put before them: judgment on what is very important, less important, or trivial; a prepared mind; and a flexible mind. The old adage "never change horses in midstream" may be good advice when on horseback in midstream but may be bad advice in science.

In Part I (47), I arbitrarily divided chance discoveries into (A) those in which chance speeded or completed a scientist's ongoing work, and (B) those in which chance changed a scientist's goals. Scientists have reported more instances of chance in the (B) category than in the (A). Why? Probably because an exciting *new* idea, concept, or experiment has usually been responsible for giant steps in science instead of small ones. But to capitalize fully on new concepts requires not only flexible scientists but also flexible science administrators and a flexible national science policy. What if the scientist, looking for a needle in a haystack and finding an ugly toad instead, was convinced he could convert it into a thing of beauty but hadn't the freedom to profit from serendipity?

Julius H. Comroe, Jr.

REFERENCES

20. Richet, C. R.: Anaphylaxis. Nobel Lecture, December 11, 1913. *Nobel Lectures, Physiology or Medicine, 1901-1921*. Elsevier, Amsterdam, 1967, pp. 473-490.
21. Dale, H. H.: Accident and opportunism in medical research. Br Med J, 1948, 2, 451-455.
22. Neil, E.: An appraisal of the work of Corneille Heymans on baroreceptor and chemoreceptor reflexes. Arch Int Pharmacodyn Ther, 1973, 202 (Supplement, pp. 283-293).
23. Kobler, J.: The Reluctant Surgeon, A Biography of John Hunter, Doubleday, Garden City, N. Y., 1960.
24. Beveridge, W. I. B.: The Art of Scientific Investigation. Random House, Vintage Books, New York, 1950.
25. Richter, C.: Experiences of a reluctant rat-catcher. The common Norway rat—friend or enemy?, Proc Am Philos Soc, 1968, 112, 403-415.
26. Astwood, E. B.: Treatment of hyperthyroidism with thiourea and thiouracil, JAMA, 1943, 122, 78-81.
27. Berson, S. A., and Yalow, R. S.: Radioimmunoassay: A status report, Hosp Prac, 1968, 3 (11), 73-83.
28. Gay, L. N., and Carliner, P. E.: The prevention and treatment of motion sickness. I. Seasickness. Johns Hopkins Hosp Med Bull, 1949, 84, 470-487.
29. Litwak, R.: The growth of cardiac surgery: Historical notes. Cardiovasc Clin, 1951, 3, 5-50. (Personal communication from F. M. Sones, Jr., see p. 38.)
30. Stead, E. A., Jr., Warren, J. V., Merrill, A. J., and Brannon, E. S.:

The cardiac output in male subjects as measured by the technique of right atrial catheterization. Normal values with observations on the effect of anxiety and tilting, J Clin Invest, 1945, 24, 326-331.
31. Sosman, M. C.: Venous catheterization of the heart. I. Indications, technics, and errors, Radiology, 1947,48, 441-450.
32a. Bing, R. J., Vandam, L. D., Gregoire, F., Handelsman, J. C., Goodale, W. T., and Eckenhoff, J. E.: Catheterization of the coronary sinus and the middle cardiac vein in man, Proc Soc Exp Biol Med, 1947, 66, 239-240.
32b. Bing, R. J., Hammond, M. M., Handelsman, J. C., Powers, S. R., Spencer, F. C., Eckenhoff, J. E., Goodale, W. T., Hafkenschiel, J. H., and Kety, S. S.: The measurement of coronary blood flow, oxygen consumption, and efficiency of the left ventricle in man, Am Heart J, 1949, 38, 1-24.
33. Berliner, R. W., Hilton, J. G., Yü, T.-F., and Kennedy, T. J., Jr.: The renal mechanism for urate excretion in man, J Clin Invest, 1950, 29, 396-401.
34. Bishop, C., Rand, R., and Talbott, J. H.: The effect of benemid (p-[di-n-propylsulfamyl]-benzoic acid) on uric acid metabolism in one normal and one gouty subject, J Clin Invest, 1951, 30, 889-895.
35. Haddow, A.: In *CIBA Foundation Symposium on Chemistry and Biology of Pteridines*, G. E. W. Wolstenholme and M. P. Cameron, ed., Churchill, London, 1954, pp. 100-103.
36. Snyder, F. F., and Rosenfeld, M.: Direct observation of intrauterine respiratory movements of the fetus and the role of carbon dioxide and oxygen in their regulation, Am J Physiol, 1937, 119, 153-166.
37. Dunn, J. S., Sheehan, H. L., and McLetchie, N. G. B.: Necrosis of the islets of Langerhans produced experimentally, Lancet, 1943, 1, 484-487.
38. Huant, E.: Note sur l'action de très fortes doses d'amide nicotinique dans les lesion bacillaires, Gas Hôp, 1945, 118, 259-260.
39. Chorine, V.: Action de l'amide nicotinique sur les bacilles du genre *Mycobacterium*, C R Acad Sci, 1945, 220, 150-151.
40. Eijkman, C.: Antineuritic vitamin and beri-beri, in *Nobel Lectures in Physiology or Medicine, 1922-1941*, Elsevier, Amsterdam, 1965, pp. 199-207.
41. Comroe, J. H., Jr.: Retrospectroscope: "Tell it like it was," Am Rev Respir Dis, 1976, 115, 667-676.
42. Comroe, J. H. Jr.: Retrospectroscope: Speculation on speculation, Am Rev Respir Dis, 1977, 115, 343-349.
43. Comroe, J. H., Jr.: Retrospectroscope: Out of the mouth of babes, Am Rev Respir Dis, 1976, 114, 1001-1009.
44. Comroe, J. H., Jr.: Retrospectroscope: The inside story, A m Rev Respir Dis, 1976, 113, 381-385.
45. Comroe, J. H., Jr.: Retrospectroscope: Whodunit (and why), Part II, Am Rev Respir Dis, 1976, 114, 229-234.
46. Lewis W. S.: Selected Letters of Horace Walpole, Yale University Press, New Haven, 1973. (See letter to Sir Horace Mann, 28 January 1754, pp. 53-57, including a photographic reproduction of Walpole's handwritten letter on p. 56.)
47. Comroe, J. H., Jr.: Retrospectroscope, Roast pig and scientific discovery, Part I, Am Rev Respir Dis, 1977, 113, 853-860.

RESPIRATORY CARE

Special Issue

Emerging Health Care Delivery Models and Respiratory Care

January 1997

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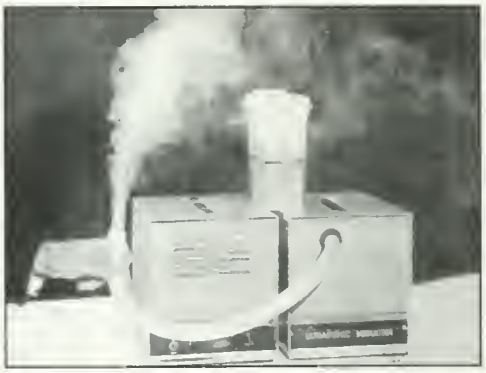
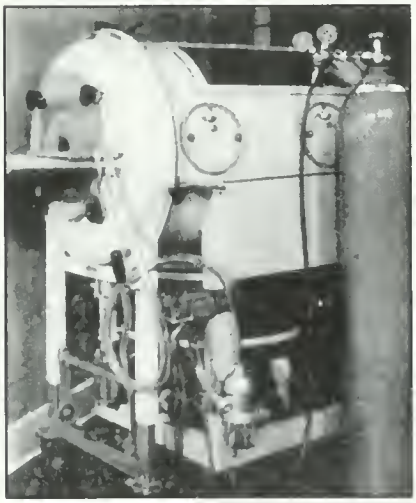
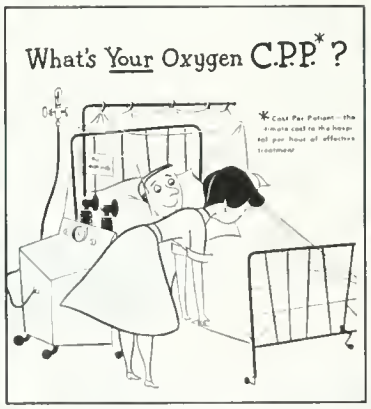


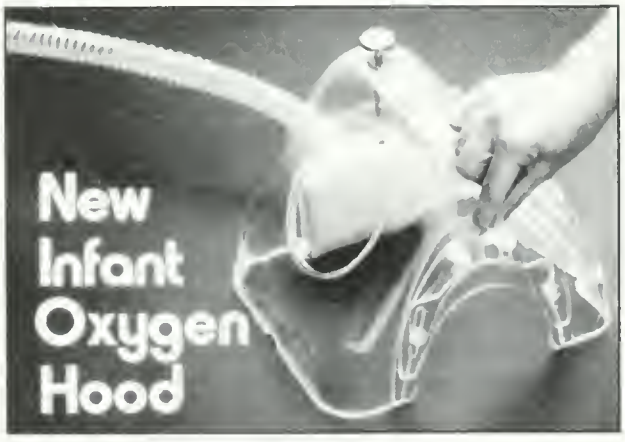
Respir Care 1964;9(5):24,
the DeVilbiss Ultrasonic Nebulizer.



The Mistogen Nebulizer adapts to the Bennett Positive Pressure Respirator of the Iron Lung, Respir Care 1957;2(1):26.

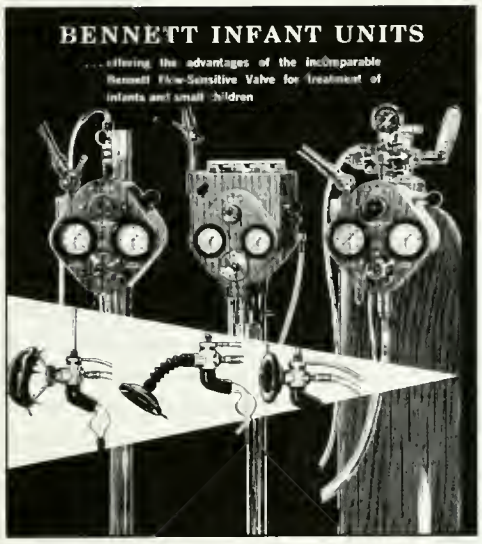


Respir Care 1957;2(1):4,
What does O_2 cost now?



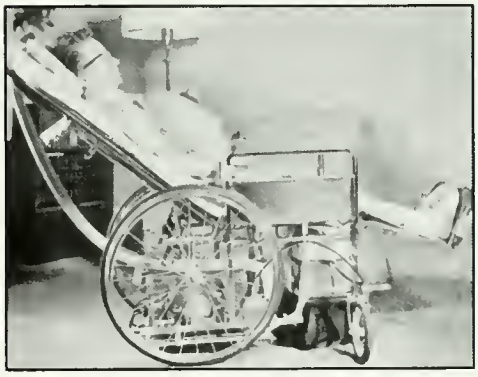
This hood featured noise supression.
from Respir Care 1976;21(5):452.

From Respir Care 1957;2(1):3.

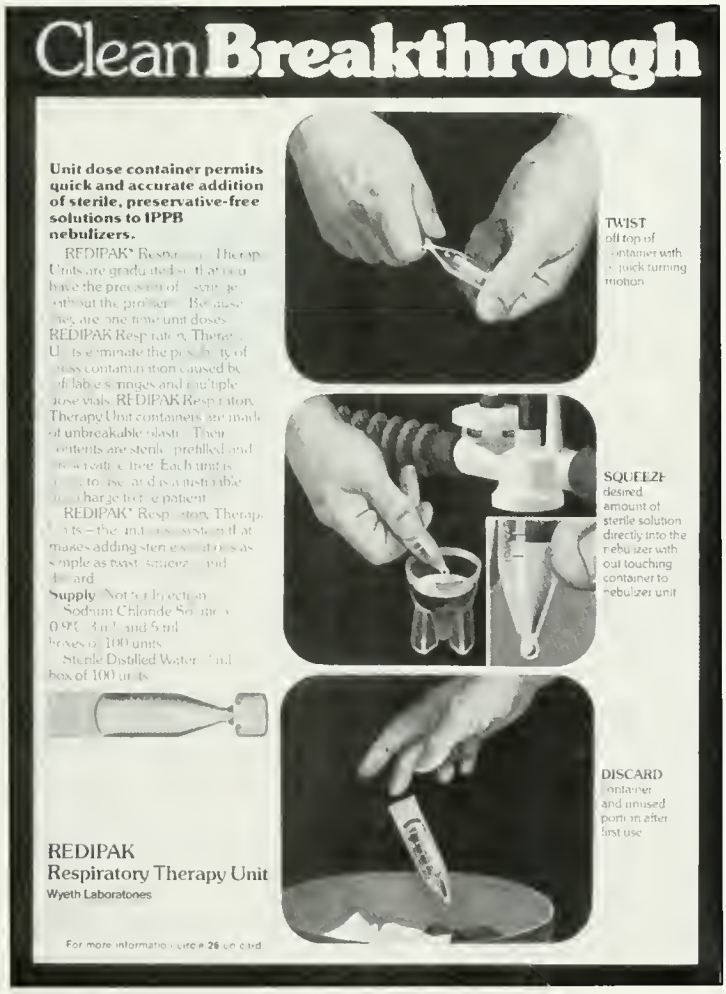

BENNETT INFANT UNITS
. . . offering the advantages of the incomparable Bennett Flow-Sensitive Valve for treatment of infants and small children

These Bennett infant units offered a flow-sensitive valve, Respir Care 1960;5(1):29.

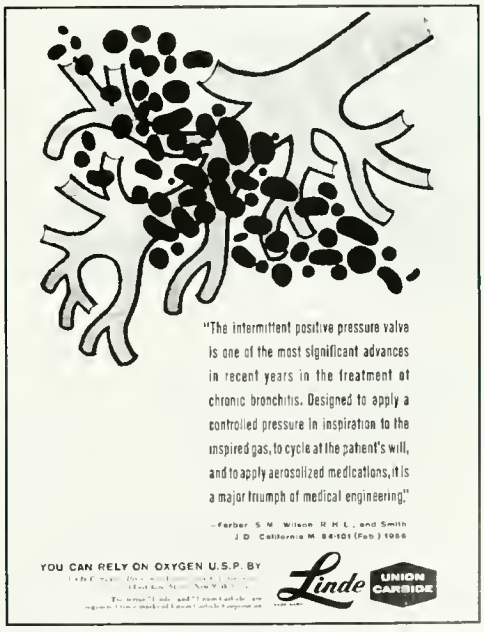
From Respir Care 1957;2(1):2.



The cuirass respirator described in Allen WC. Therapists must become more expert as use of respiratory aids grow, Respir Care 1960;5(1):20-28.


Clean Breakthrough
Unit dose container permits quick and accurate addition of sterile, preservative-free solutions to IPPB nebulizers.
TWIST off top of container with a quick turning motion
SQUEEZE desired amount of sterile solution directly into the nebulizer with out touching container to nebulizer unit
DISCARD container and unused porti on after first use
REDIPAK
Respiratory Therapy Unit
Wyeth Laboratories

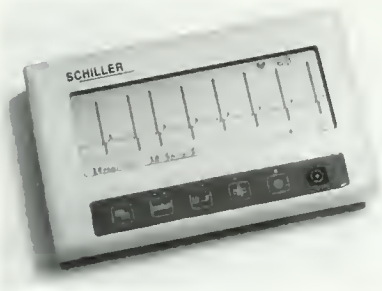
From Respir Care 1976;21(5):433.


"The intermittent positive pressure valve is one of the most significant advances in recent years in the treatment of chronic bronchitis. Designed to apply a controlled pressure in inspiration to the inspired gas, to cycle at the patient's will, and to apply aerosolized medications, it is a major triumph of medical engineering."
YOU CAN RELY ON OXYGEN U.S.P. BY
Linde
UNION CARBIDE

This intermittent positive pressure valve ad cited a 1956 article, Respir Care 1960:5(1):25.

New Products & Services

News releases about new products and services will be considered for publication in this section. There is no charge for these listings. Send descriptive release and glossy black and white photographs to RESPIRATORY CARE Journal, New Products and Services Dept, 11030 Ables Lane, Dallas TX 75229-4593. The Reader Service Card immediately follows the authors & advertisers index at the back of the Journal.



POCKET-SIZE ELECTROCARDIOGRAPH. Schiller America announces the Miniscope MS-3, pocket-size electrocardiograph (ECG). By holding the MS-3 against the patient's chest, the health-care practitioner can view up to 47 seconds of ECG information and real-time heart rate on the unit's screen, the company claims. The ECG's built-in tripod electrode eliminates the need for standard electrode hook-ups and reduces time and costs. The unit has a 30-minute memory and can record data for 2 separate patients. Data from the MS-3 can be transferred to personal computers, allowing for review, validation, archiving, and printing. For details about the unit, circle Reader Service Number 160.

MEDICAL GAS HANDBOOK. Modern Medical Systems Company publishes *Medical Gas Utility Program*—a handbook of medical gases and delivery systems. The company says that the book was 2 years in development and contains more than 300 pages, 20 checklists, and 120 charts and tables. The safety training section is a complete training program that meets all Joint Commission for the Accreditation of Healthcare Organization requirements. Yearly upgrades are available. For details, circle Reader Service Number 161.

CARDIOLOGY WORKSTATION. The Portrait™ cardiology workstation is now available from Mortara Instruments. The station can be customized to record resting electrocardiograms (ECGs) including the unique 3 + 3 format that includes 12 leads and 3 rhythm strips; the Portrait stores 300 ECGs. When upgraded to include stress testing, the workstation stores 20 different exercise protocols and offers full disclosure final reports. As a Holter system, the unit offers a 12-lead system that reports ECGs and rhythm strips. When all 3 aspects are combined, the company claims that the Portrait is a powerful and flexible diagnostic tool. Visit Mortara's Internet site at http//www.mortara.com or circle Reader Service Number 162 for more information.

GENERAL PURPOSE CLEANER. Cetylite Industries Inc releases General Purpose Ultrasonic Cleaner. Cetylite claims that the cleaner is effective for removing debris, compounds, body fluids, and blood from metal, glass, porcelain, precious and semiprecious metals, plastic, and rubber. The concentrated cleaner is available in a 32-ounce metered-dose squeeze bottle that, when mixed with water, will produce 32 gallons of cleaning solution. The product is environmentally safe for disposal in drains. For more information, circle Reader Service Number 163.

ALLERGY REFERENCE BOOK. Omnigraphics Inc publishes *Allergies Sourcebook*, a 600-page reference to chronic respiratory problems, skin rashes, asthma, and anaphylactic shock. The book is written for those with allergic conditions and provides information about allergic triggers, symptoms, treatments, coping strategies, and current research, the publisher says. The book uses data provided by the National Institutes of Health and its subagencies and the Food and Drug Administration. The book also provides a glossary and an index. For information on how to obtain a copy of the book, circle Reader Service Number 164.

MONITORING SCALE. Ferraris Medical Inc offers an improved scale for the Mark 14 Wright Respirometer. The monitoring scale now has 0.1-L graduations subdivided into 10-mL divisions for more accurate readings of tidal and minute volumes. According to Ferraris, the Mark 14 retains the accuracy of ± 2% at 15 L/min and features the convenient on-off slide switch for locking and reset button. The Mark 14 also comes with 3 circuit adapters, a safety harness, and a fully padded carrying case. Circle Reader Service Number 165 for details.

American Association for Respiratory Care Membership Application

Please read the eligibility requirements for each of the classifications in the right-hand column, then complete the applicable section. All information requested below must be provided, except where indicated as optional. See other side for more information and fee schedule. Please sign and date application on reverse side and type or print clearly. Processing of application takes approximately 15 days.

- Active
- Associate
  - Foreign
  - Physician
  - Industrial
- Special
- Student

Last Name _____

First Name _____ Middle _____

Social Security No. _____

Home Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Primary Job Responsibility (check one only)

- Technical Director
- Assistant Technical Director
- Pulmonary Function Specialist
- Instructor/Educator
- Supervisor
- Staff Therapist
- Staff Technician
- Rehabilitation/Home Care
- Medical Director
- Sales
- Student
- Other, specify _____

Type of Business

- Hospital
- Skilled Nursing Facility
- DME/HME
- Home Health Agency
- Educational Institution
- Manufacturer or supplier
- Other, specify _____

Date of Birth (optional) _____ Sex (optional) _____

U.S. Citizen? ___ Yes ___ No

Have you ever been a member of the AARC? _____

If so, when? From _____ to _____

Preferred mailing address: Home Business

FOR ACTIVE MEMBER

An individual is eligible if he/she lives in the U.S. or its territories or was an Active Member prior to moving outside its borders or territories, and meets ONE of the following criteria (1) is legally credentialed as a respiratory care professional if employed in a state that mandates such, OR (2) is a graduate of an accredited educational program in respiratory care, OR (3) holds a credential issued by the NBRC. An individual who is an AARC Active Member in good standing on December 8, 1994 will continue as such provided his/her membership remains in good standing

Place of Employment _____

_____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Medical Director/Medical Sponsor _____

FOR ASSOCIATE OR SPECIAL MEMBER

Individuals who hold a position related to respiratory care but do not meet the requirements of Active Member shall be Associate Members. They have all of the rights and benefits of the Association except to hold office, vote, or serve as chair of a standing committee. The following subclasses of Associate Membership are available. Foreign, Physician, and Industrial (individuals whose primary occupation is directly or indirectly devoted to the manufacture, sale, or distribution of respiratory care equipment or supplies). Special Members are those not working in a respiratory care-related field

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE.

Place of Employment _____

_____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

FOR STUDENT MEMBER

Individuals will be classified as Student Members if they meet all the requirements for Associate Membership and are enrolled in an educational program in respiratory care accredited by, or in the process of seeking accreditation from, an AARC-recognized agency

SPECIAL NOTICE — Student Members do not receive Continuing Respiratory Care Education (CRCE) transcripts. Upon completion of your respiratory care education, continuing education credits may be pursued upon your reclassification to Active or Associate Member.

School/RC Program _____

_____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Length of Program

1 year 4 years

2 years Other, specify_____

Expected Date of Graduation (REQUIRED INFORMATION)

Month_____ Year_____

American Association for Respiratory Care • 11030 Ables Lane • Dallas, TX 75229-4593 • (972) 243-2272 • Fax (972) 484-2720

American Association for Respiratory Care Membership Application

Demographic Questions

We request that you answer these questions in order to help us design services and programs to meet your needs.

Check the Highest Degree Earned

- ☐ High School
- ☐ RC Graduate Technician
- ☐ Associate Degree
- ☐ Bachelor's Degree
- ☐ Master's Degree
- ☐ Doctorate Degree

Number of Years in Respiratory Care

- ☐ 0-2 years
- ☐ 3-5 years
- ☐ 6-10 years
- ☐ 11-15 years
- ☐ 16 years or more

Job Status

- ☐ Full Time
- ☐ Part Time

Credentials

- ☐ RRT
- ☐ CRTT
- ☐ Physician
- ☐ CRNA
- ☐ RN
- ☐ LVN/LPN
- ☐ CPFT
- ☐ RPFT
- ☐ Perinatal/Pediatric

Salary

- ☐ Less than $10,000
- ☐ $10,001-$20,000
- ☐ $20,001-$30,000
- ☐ $30,001-$40,000
- ☐ $40,001 or more

PLEASE SIGN

I hereby apply for membership in the American Association for Respiratory Care and have enclosed my dues. If approved for membership in the AARC, I will abide by its bylaws and professional code of ethics. I authorize investigation of all statements contained herein and understand that misrepresentations or omissions of facts called for is cause for rejection or expulsion.

A yearly subscription to **Respiratory Care** journal and **AARC Times** magazine includes an allocation of $6.50 from my dues for each of these publications.

NOTE: Contributions or gifts to the AARC are not tax deductible as charitable contributions for income tax purposes. However, they may be tax deductible as ordinary and necessary business expenses subject to restrictions imposed as a result of association lobbying activities. The AARC estimates that the nondeductible portion of your dues - the portion which is allocable to lobbying - is 26%.

Signature _____

Date _____

Membership Fees

Payment must accompany your application to the AARC. Fees are for 12 months. (NOTE: Renewal fees are $65.00 Active, Associate-Industrial or Associate-Physician, or Special status; $80.00 for Associate-Foreign status; and $35.00 for Student status.)

☐ Active	$77.50
☐ Associate (Industrial or Physician)	$77.50
☐ Associate (Foreign)	$92.50
☐ Special	$77.50
☐ Student	$35.00
TOTAL	$_____

Specialty Sections

Established to recognize the specialty areas of respiratory care. The sections publish a newsletter four times a year that focuses on issues of specific concern to that specialty. The sections also design the specialty programming at the national AARC meetings.

☐ Adult Acute Care Section	$ 5.00
☐ Education Section	$10.00
☐ Perinatal-Pediatric Section	$ 5.00
☐ Diagnostics Section	$ 5.00
☐ Continuing Care-Rehabilitation Section	$ 5.00
☐ Management Section	$10.00
☐ Transport Section	$ 5.00
☐ Home Care	$ 5.00
☐ Subacute Care	$ 5.00
TOTAL	$_____

GRAND TOTAL = Membership Fee plus optional sections $_____

☐ Total Amount Enclosed $_____

☐ Please charge my dues (see below)

To charge your dues, complete the following:

- ☐ MasterCard
- ☐ Visa

Card Number

_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Card Expires _____/_____

Signature _____

Mail application and appropriate fees to:
American Association for Respiratory Care • 11030 Ables Lane • Dallas, TX 75229-4593 • (972) 243-2272 • Fax (972) 484-2720

1997 Call for Abstracts

RESPIRATORY CARE • OPEN FORUM

The American Association for Respiratory Care and its science journal, RESPIRATORY CARE, invite submission of brief abstracts related to any aspect of cardiorespiratory care. The abstracts will be reviewed, and selected authors will be invited to present posters at the OPEN FORUM during the AARC International Convention and Exhibition in New Orleans, Louisiana, December 6-9, 1997. Accepted abstracts will be published in the November 1997 issue of RESPIRATORY CARE. Membership in the AARC is not required for participation.

SPECIFICATIONS—READ CAREFULLY!

An abstract may report **(1) an original study, (2) the evaluation of a method, device or protocol, or (3) a case or case series.** Topics may be aspects of adult acute care, continuing care/rehabilitation, perinatology/pediatrics, cardiopulmonary technology, or health care delivery. The abstract may have been presented previously at a local or regional—but not national—meeting and should not have been published previously in a national journal. The abstract is the only evidence by which the reviewers can decide whether the author should be invited to present a poster at the OPEN FORUM. Therefore, *the abstract must provide all important data, findings, and conclusions.* Give specific information. Do not write such general statements as "Results will be presented" or "Significance will be discussed."

Essential Content Elements

Original study. Abstract *must* include (1) Background: statement of research problem, question, or hypothesis; (2) Method: description of research design and conduct in sufficient detail to permit judgment of validity; (3) Results: statement of research findings with quantitative data and statistical analysis; (4) Conclusions: interpretation of the meaning of the results.

Method, device, or protocol evaluation. Abstract *must* include (1) Background: identification of the method, device, or protocol and its intended function; (2) Method: description of the evaluation in sufficient detail to permit judgment of its objectivity and validity; (3) Results: findings of the evaluation; (4) Experience: summary of the author's practical experience or a lack of experience; (5) Conclusions: interpretation of the evaluation and experience. Cost comparisons should be included where possible and appropriate.

Case report. Abstract *must* report a case that is uncommon or of exceptional educational value and must include (1) Introduction: Relevant basic information important to understanding the case. (2) Case Summary: Patient data and response, details of interventions. (3) Discussion: Content should reflect results of literature review. The author(s) should have been actively involved in the case and a case-managing physician must be a co-author or must approve the report.

Abstract Format and Typing Instructions

Accepted abstracts will be photographed and reduced by 40%; therefore, the size of the original text should be *at least* 10 points. A font like Helvetica or Geneva makes the clearest reproduction. The first line of the abstract should be the title in all capital letters. Title should explain content. Follow title with names of all authors (including credentials), institution(s), and location; underline presenter's name. Type or electronically print the abstract *single spaced in a single paragraph in the space provided on the abstract blank.* Insert only one letter space between sentences. Text submission on diskette is encouraged but must be accompanied by a hard copy. Identifiers will be masked (blinded) for review. Data may be submitted in table form, *and simple figures may be included provided they fit within the space allotted.* No figures, illustrations, or tables are to be attached to the abstract form. Provide all author information requested. A clear photocopy of the abstract form may be used. Standard abbreviations may be employed without explanation; new or infrequently used abbreviations should be spelled out on first use. Any recurring phrase or expression may be abbreviated, if it is first explained. Check the abstract for (1) errors in spelling, grammar, facts, and figures; (2) clarity of language; and (3) conformance to these specifications. An abstract not prepared as requested may not be reviewed. Questions about abstract preparation may be telephoned to the editorial staff of RESPIRATORY CARE at (972) 406-4667.

Deadline Allowing Revision

Authors may choose to submit abstracts early. Abstracts postmarked by March 17, 1997 will be reviewed and the authors notified *by letter only* to be mailed by April 25, 1997. Rejected abstracts will be accompanied by a written critique that should, in many cases, enable authors to revise their abstracts and resubmit them by the final deadline (May 27, 1997).

Final Deadline

The mandatory Final Deadline is May 27, 1997 (postmark). Authors will be notified of acceptance or rejection *by letter only*. These letters will be mailed by August 15, 1997.

Mailing Instructions

Mail (Do not fax!) 2 clear copies of the completed abstract form, diskette (if possible), and a stamped, self-addressed postcard (for notice of receipt) to:

RESPIRATORY CARE OPEN FORUM
11030 Ables Lane
Dallas TX 75229-4593

1997 Respiratory Care Open Forum
Abstract Form

18.8 cm or 7.4"

13.9 cm or 5.5"

1. Title must be in all upper case (capital) letters, authors' full names and text in upper and lower case.
2. Follow title with all authors' names including credentials (underline presenter's name), institution, and location.
3. Do not justify (ie, leave a 'ragged' right margin).
4. **Do not use type size less than 10 points.**
5. All text, tables, and figures must fit into the rectangle shown.
6. Submit 2 clean copies. This form may be photocopied if multiple abstracts are to be submitted.

Mail original & 1 photocopy (along with postage-paid postcard) to

Respiratory Care Open Forum
11030 Ables Lane
Dallas TX 75229-4593

Early deadline is March 17, 1997 (postmark)

Final deadline is May 27, 1997 (postmark)

Presenter

Name & Credentials

Mailing Address

Voice Phone & Fax

Corresponding Author if Different from Presenter

Name & Credentials

Mailing Address

Voice Phone & Fax

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For VOLUNTARY reporting by health professionals of adverse events and product problems

Page of

Form Approved OMB No. 0910-0291 Expires 4/30/98
See OMB statement on reverse

FDA Use Only (Resp Care)

Triage unit sequence #

A. Patient information

1. Patient identifier
In confidence

2. Age at time of event:
or
Date of birth:

3 Sex
☐ female
☐ male

4 Weight
lbs
or
kgs

B. Adverse event or product problem

1 ☐ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)

2 Outcomes attributed to adverse event (check all that apply)
☐ death (mo day yr)
☐ life-threatening
☐ hospitalization – initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other

3. Date of event (mo day yr)

4 Date of this report (mo day yr)

5 Describe event or problem

6. Relevant tests/laboratory data, including dates

7 Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1 Name (give labeled strength & mfr/labeler, if known)
#1
#2

2 Dose, frequency & route used
#1
#2

3. Therapy dates (if unknown, give duration) (from to / best estimate)
#1
#2

4 Diagnosis for use (indication)
#1
#2

5 Event abated after use stopped or dose reduced
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

6 Lot # (if known)
#1
#2

7 Exp. date (if known)
#1
#2

8 Event reappeared after reintroduction
#1 ☐ yes ☐ no ☐ doesn't apply
#2 ☐ yes ☐ no ☐ doesn't apply

9 NDC # (for product problems only)
– –

10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1 Brand name

2. Type of device

3 Manufacturer name & address

4 Operator of device
☐ health professional
☐ lay user/patient
☐ other

5. Expiration date (mo day yr)

6
model #
catalog #
serial #
lot #
other #

7 If implanted, give date (mo day yr)

8 If explanted, give date (mo day yr)

9 Device available for evaluation? (Do not send to FDA)
☐ yes ☐ no ☐ returned to manufacturer on (mo day yr)

10 Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1 Name & address

phone #

2 Health professional?
☐ yes ☐ no

3 Occupation

4 Also reported to
☐ manufacturer
☐ user facility
☐ distributor

5 If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH
5600 Fishers Lane
Rockville, MD 20852-9787

or FAX to:
1-800-FDA-0178

FDA Form 3500 1/96)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ADVICE ABOUT VOLUNTARY REPORTING

Report experiences with:

- medications (drugs or biologics)
- medical devices (including in-vitro diagnostics)
- special nutritional products (dietary supplements, medical foods, infant formulas)
- other products regulated by FDA

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- death
- life-threatening (real risk of dying)
- hospitalization (initial or prolonged)
- disability (significant, persistent or permanent)
- congenital anomaly
- required intervention to prevent permanent impairment or damage

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report product problems – quality, performance or safety concerns such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labeling
- therapeutic failures

How to report:

- just fill in the sections that apply to your report
- use section C for all products except medical devices
- attach additional blank pages if needed
- use a separate form for each patient
- report either to FDA or the manufacturer (or both)

Important numbers:

- 1-800-FDA-0178 to FAX report
- 1-800-FDA-7737 to report by modem
- 1-800-FDA-1088 to report by phone or for more information
- 1-800-822-7967 for a VAERS form for vaccines

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise. However, FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act.

The public reporting burden for this collection of information has been estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to.

DHHS Reports Clearance Office
Paperwork Reduction Project (0910-0291)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number

Please do NOT return this form to either of these addresses.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • Food and Drug Administration

FDA Form 3500-back

Please Use Address Provided Below – Just Fold In Thirds, Tape and Mail

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Rockville, MD 20857

Official Business
Penalty for Private Use $300

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES OR APO FPO

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO. 946 ROCKVILLE, MD

POSTAGE WILL BE PAID BY FOOD AND DRUG ADMINISTRATION

MEDWATCH
The FDA Medical Products Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

Not-for-profit organizations are offered a free advertisement of up to eight lines to appear, on a space-available basis, in Calendar of Events in RESPIRATORY CARE. Ads for other meetings are priced at $5.50 per line and require an insertion order. Deadline is the 20th of the month two months preceding the month in which you wish the ad to run. Submit copy and insertion orders to Calendar of Events, RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229-4593.

Calendar of Events

AARC & AFFILIATES

November 14—The South District of the Texas Society
The Victoria District presents the Fall Seminar in Victoria, Texas.
Contact: Dennis Albrecht, Citizen's Medical Center, at (512) 573-9181.

November 15—The South Region of the Texas Society
"One Stop Shop CRCE Express" in Houston, Texas. CRCE: 6 credit hours have been requested.
Contact: Kerri Poole at (409) 945-9761.

November 15—The Puget Sound Chapter of the Washington Society
18th Annual Adult Critical Care Conference at the Urban Horticulture Center of the University of Washington campus, Seattle, Washington.
Contact: Deb Jones at (206) 548-4445.

December 10—AARC Video Conference
"Airway Management: Tricks of the Trade." The final segment of the 1996 7-part video conference "Professor's Rounds in Respiratory Care," from 12:30 to 2 p.m. Eastern Time. Live telephone question-and-answer session airs Dec. 19.
CRCE: 1 credit hour.
Contact: AARC at (972) 243-2272.

January 29-31, 1997—The Oregon Society
Annual Pacific Northwest Respiratory Care Conference at the Monarch Hotel and Conference Center in Clackamas, Oregon.
Exhibitors Contact: Tami Carter at (503) 626-9947. Contact: Irene Iwata-Morgan at (503) 494-6158.

January 31, 1997—The Texas Society
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March 5–7, 1997—Journées Internationales de Ventilation à Domicile (JIVD)
6th International Conference on Home Mechanical Ventilation, sponsored by the AARC and JIVD, in Lyon, France.
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Abstracts are due by Dec. 15.
For guidelines on abstract submissions and for more information on the conference, contact the Congress Secretariat at JIVD, Hôpital de la Croix Rousse, Service de Réanimation Médicale et Assistance Respiratoire, 93 Grande Rue de la Croix Rousse, 69317 Lyon Cedex 04, France, or call (33) 78 39 08 43, fax (33) 78 39 58 63, or send E-mail to 100732.3540 @compuserve.com.

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Notices

Notices of competitions, scholarships, fellowships, examination dates, new educational programs, and the like will be listed here free of charge. Items for the Notices section must reach the Journal 60 days before the desired month of publication (January 1 for the March issue, February 1 for the April issue, etc). Include all pertinent information and mail notices to RESPIRATORY CARE Notices Dept, 11030 Ables Lane, Dallas TX 75229-4593.

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Radiometer Awards for Best Features

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Cardiorespiratory Interactions—The Role of Echocardiography in the Practice of Respiratory Care—A Resai Bengur, Jon N Meliones, James W NeSmith, Michele E Kappeler, and Jennifer S Li. [Respir Care 1996;41(3):215-225]

Test Your Radiologic Skill—Right Paratracheal Density in an Asymptomatic Patient—Luis Teba and N LeRoy Lapp. [Respir Care 1996;41(6):544-547]

PFT Corner—Lessons from Spirometry: Look at the Picture—Matthew Veatch, Jack Wanger, and Edward Chan. [Respir Care 1996;41(8):745-747]

GlaxoWellcome 1996 OPEN FORUM Awards

Best Papers based on OPEN FORUM Presentations by Those Who Have Never Published as First Author
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Accuracy of Electrolyte and Blood Gas Determinations from Samples Collected in Preheparinized Syringes—Virginia M Haver, William Eng, John Douglas Hussey, Daniel D Bankson, and Sambasiva Lakshminarayan. [Respir Care 1996;41(9):805-808]

Regulation of Pressurization Rate Reduces Inspiratory Effort during Pressure Support Ventilation: A Bench Study—Massimo Croci, Paolo Pelosi, Davide Chiumello, and Luciano Gattinoni. [Respir Care 1996;41(10):880-884]

Best Paper Based on an OPEN FORUM Presentation
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Original Study, Evaluation, or Case Report
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A Respiratory Care Assessment-Treatment Program: Results of a Retrospective Study—Kevin L Shrake, John E Scaggs, Kevin R England, Joseph Q Henkle, and Lanie E Eagleton. [Respir Care 1996;41(8):703-713]

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Comparison of Three Humidification Techniques during Mechanical Ventilation: Patient Selection, Cost, and Infection Considerations—Richard D Branson, Kenneth Davis Jr, Richard Brown, and Mitchell Rashkin. [Respir Care 1996;41(9):809-816]

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	July 12, 1997 Application Deadline: May 1, 1997	100 60	(new applicant) (reapplicant)
	November 8, 1997 Application Deadline: September 1, 1997	100 60	(new applicant) (reapplicant)
RRT Examination	June 7, 1997 Application Deadline: February 1, 1997	100 60	Written only (new applicant) Written only (reapplicant)
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	December 6, 1997 Application Deadline: August 1, 1997	210 170	Both (new applicant) Both (reapplicant)
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8. ❑ Management

IV.Position
A. ❑ Dept Head
B. ❑ Chief Therapist
C. ❑ Supervisor
D. ❑ Staff Technician
E. ❑ Staff Therapist
F. ❑ Educator
G. ❑ Medical Director
H. ❑ Anesthesiologist
I. ❑ Pulmonologist
J. ❑ Other MD
K. ❑ Nurse

V. Are you a member of the AARC?
1 ❑ Yes 2. ❑ No

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1. ❑ Hosp 500 or more beds
2. ❑ Hosp 300 to 499 beds
3. ❑ Hosp 200 to 299 beds
4. ❑ Hosp 100 to 199 beds
5. ❑ Hosp 100 or less beds
6. ❑ Skilled Nursing Facility
7. ❑ Home Care Practice
8. ❑ School

II. Department
A. ❑ Respiratory Therapy
B. ❑ Cardiopulmonary
C. ❑ Anesthesia Service
D. ❑ Emergency Dept

III. Specialty
1. ❑ Clinical Practice
2. ❑ Perinatal Pediatrics
3. ❑ Critical Care
4. ❑ Clinical Research
5. ❑ Pulmonary Function Lab
6. ❑ Home Care/Rehab
7. ❑ Education
8. ❑ Management

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1. ❑ Yes 2. ❑ No

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